



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT OPERATION

In re application of:

Sriwongjanya et al.

Appl. No.: 10/617,456

Group Art Unit: 1615

Filed: July 11, 2003

Examiner: Susan T. Tran

FOR: FORMULATION AND PROCESS FOR DRUG LOADED CORES

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR 1.131

Samuel Yuk declares and states as follows:

1. I am one of the named inventors in the above-identified application, assigned to Pharmaceuticals, LLC.
2. I have read and am familiar with the Office Action dated March 9, 2007, in the above-identified application. A copy of which is attached hereto as Exhibit A. I understand that the Examiner has rejected Claims 1, 3-6, 8, 9, 12, 13, 17-20, 27, 28, 30-32 and 64 under 35 U.S.C. §102(e) in view of United States Patent No. 7,022,342 and claims 1, 3-6, 8, 9, 12, 13, 17-23, 27-49, 51-54, 56, 57 and 60-64 under 35 U.S.C. § 103(a) in view of the same patent. A copy of United States Patent No. 7,022,342 is attached hereto as Exhibit B.
3. I have been informed by the attorneys responsible for the prosecution of this application that the earliest effective date of said United States Patent No. 7,022,342 is March 28, 2002.
4. Prior to March 28, 2002, the invention described in the above-identified application (Application No. 10/671,456) was completed in the United States of America.

Application No. 10/617,456 was filed less than sixteen months after the earliest effective filing date of United States Patent No. 7,022,342.

5. Well prior to March 28, 2002, Mongol Sriwongjanya, Avinash Nangia and I (hereinafter “the inventors”) were involved in the development of a controlled release formulation for metoprolol succinate. Many of the formulations disclosed in United States Patent No. 10/617,456 were developed prior to March 28, 2002. Specifically, the idea to use drug layered water soluble or water swellable cores was made by the inventors prior to March 28, 2002. Further, the inventors had the idea to coat the drug layered cores with a water insoluble film forming polymer and a channeling agent prior to March 28, 2002. As evidence in support of the averments in this paragraph and in paragraph 4, above, attached hereto as Exhibit C is a copy of a set of Batch Records from Andrx Pharmaceuticals, Inc. with the dates redacted describing work the inventors performed in Florida prior to March 28, 2002.

6. The Batch Records attached as Exhibit C explicitly describe sugar spheres (water soluble core) being coated with metoprolol succinate (active), hydroxypropyl methylcellulose (binder) and polysorbate 80 (surfactant) to form active pellets (see Lot # P02005). Next the active pellets are coated with methacrylic acid copolymer (channeling agent), cellulose acetate butyrate (water insoluble film forming polymer) and poloxamer (emulsifier) to form extended release pellets (See Lot # P02014).

More specifically, a process wherein 0.45 kg of hydroxypropyl methylcellulose (Methocel E-5) was dissolved in 27.0 kg of purified water using a mechanical stirrer until a clear solution was obtained. 9.0 kg of metoprolol succinate and 0.012 kg of Tween 80 were then added into the solution.

5.40 kg of sugar spheres NF 60/80 were placed into a fluidized bed coater. The drug suspension prepared above was sprayed onto the sugar spheres using the following parameter:

Nozzle tip diameter	1.2 mm
Screen Size	100 mesh
Shaking interval	30 min
Shaking Duration	3 sec
Atomization Pressure	2.5 bar
Inlet Air Temperature	50-100°C
Pump Rate	5-80 mL/min
Tubing Size	16 mm

Once the drug suspension was consumed, the pellets were dried for 10 minutes in the fluidized bed coater or until the loss on drying (LOD) was less than 3%.

In the next step, Batch Record P02013, a second drug layer is applied to the product of P02005. Specifically, a second drug coat suspension was prepared by dissolving 0.35 kg of hydroxypropyl methylcellulose (Methocel E-5) in 21.00 kg of purified water using a mechanical stirrer until a clear solution was obtained. 7.00 kg of metoprolol succinate and 0.009 kg of Tween 80 was then added into the solution.

5.78 kg of metoprolol active pellets from the first drug layering step (P02005) were placed into a fluidized bed coater. Then the second drug coating suspension was sprayed onto the active pellets of P02005 using the parameters set forth above.

After the drug suspension was consumed the pellets were dried for 10 minutes or until the loss on drying (LOD) was less than 3%. Finally, the pellets were screened using 40 mesh and 80 mesh screens. The pellets between the 40 and 80 mesh were collected.

Next, Batch Record P02014 describes the extended release coating of the active pellets as follows:

The controlled release coating was prepared by dissolving 1.908 kg of the cellulose acetate butyrate, 0.137 kg of the Eudragit® S100, and 0.227 kg of the Lutrol F-68 into a mixture of 4.2 kg of purified water and 37.8 kg of acetone and stirred until the solution was clear using a mechanical stirrer. The solution was then applied to the drug layered pellets (P02013) prepared above using the bottom spray fluidized bed coater with the same parameters described in the drug layer step above.

After the controlled release solution was consumed the pellets were dried for 10 minutes or until the LOD was less than 3%. Finally, pellets were screened through 25 and 80 mesh screens and the pellets between the 25 and 80 mesh screens were collected.

7. Dissolution testing was conducted on the extended release pellets (P02014) to ensure that the above controlled release tablets released metoprolol succinate in a controlled manner over an extended period of time. The results of this dissolution testing are attached hereto as Exhibit D.

8. Attached as Exhibit E are portions of Laboratory Notebook No. SR 1860, assigned to inventor Mongol Sriwongjanya with the dates redacted. This laboratory notebook contains work done for Andrx in Florida, USA. The work done in this notebook all occurred before March 28, 2002. This notebook describes the use of CELPHERE®, which is tradename for microcrystalline cellulose spheres, which are water swellable cores. These cores were spray coated in a uniglatt fluidized bed coater with a drug suspension coating comprising metoprolol succinate, METOCEL® E5 (which is the tradename for hydroxypropyl methylcellulose), and TWEEN® 80 (which is the tradename for polysorbate 80) (see pages 31-33, 42). These CELESPHERE® drug coated cores were then coated with a controlled release coating containing CAB (cellulose acetate butyrate, a water insoluble film forming polymer), ATBC (acetyltributyl citrate, a channeling agent) or PEG (polyethylene glycol, a channeling agent) (See pages 34-47).

9. The controlled release CELLSPHERE® pellets described on pages 31-47 were tested to ensure that the above controlled release tablets released metoprolol succinate in a controlled manner over an extended period of time. The results of this dissolution testing are attached hereto as Exhibit F.

10. Exhibit E also describes work performed prior to March 28, 2002 in which 60/80 sugar spheres (see page 62) were spray coated in a UniGlatt fluidized bed coater with a drug suspension coating comprising metoprolol succinate, METOCEL® E5 (which is the tradename for hydroxypropyl methylcellulose), and TWEEN® 80 (which is the tradename for polysorbate 80). These 60/80 coated drug cores are then coated with controlled release CAB (cellulose acetate butyrate, a water insoluble film forming

polymer), HPC (hydroxypropyl cellulose, a channeling agent) and Lutrol F-68 (poloxamer, an emulsifying agent) (see pages 71-72 and 74-75).

11. The controlled release 60/80 drug coated sugar spheres described on pages 62, 71-72 and 74-75 were tested to ensure that the above controlled release tablets released metoprolol succinate in a controlled manner over an extended period of time. The results of this dissolution testing are attached hereto as Exhibit G.

I further declare that all statements made herein of my own knowledge are true and that all statements made of information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

05/29/07
Date


Samuel Yuk



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,456	07/11/2003	Mongkol Sriwongjanya	141-287	3239

47888	7590	03/09/2007
HEDMAN & COSTIGAN P.C.		
1185 AVENUE OF THE AMERICAS		
NEW YORK, NY 10036		

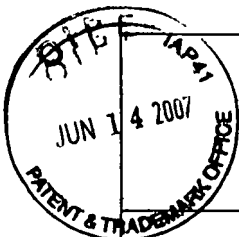
EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.



Office Action Summary

Application No.

10/617,456

Applicant(s)

SRIWONGJANYA ET AL.

Examiner

Susan T. Tran

Art Unit

1615

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-49 and 51-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-49 and 51-64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 is rejected for failing to further limit the subject matter of claim 1. Claim 1 has already recited the limitation "channeling agent".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-6, 8, 9, 12, 13, 17-20, 27, 28, 30-32 and 64 are rejected under 35 U.S.C. 102(e) as being anticipated by Chen et al. USPN 7,022,342.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome

either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Chen discloses an oral controlled release capsule comprising: 1) a core comprising a β -adrenergic blocking agent, an inert pellet, a binder, and a filler; and 2) a coating comprising a water-insoluble polymer, a water soluble polymer, a plasticizer, and an anti-sticking agent (column 1, lines 8-18; and column 3, lines 6-30). β -adrenergic blocking agent includes metoprolol. Inert pellet as a starting material can be any type of commonly known pellet including starch or sugar sphere having diameter from about 15-50 mesh. Binder includes hydroxypropyl methylcellulose (column 4, lines 16-42). Water-insoluble polymer includes cellulose acetate butyrate. Plasticizing agent includes well-known pharmaceutically acceptable agents (column 5, lines 10-56). Chen further discloses the process for preparing the oral controlled release dosage form comprising forming a suspension of the binder, drug and other ingredients, layering the suspension onto the inert pellet using any of the layering techniques known in the art such as fluidized bed coating, rotor granulation or pan coating, and layering the controlled release coating layer by any means commonly known in the art (column 5, lines 3-9, and 57-64). The claimed release profiles, as well as the C_{max} values are disclosed in columns 6 and 9.

It is noted that independent claims 1 and 49 require channeling agent. However, the specific channeling agent is not recited in these claims. Therefore, any other

additives/excipients such as filler having particle size of about 20 μ m anticipated the claimed channeling agent (column 4, lines 48-51).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-6, 8, 9, 12, 13, 17-23, 27-49, 51-54, 56, 57 and 60-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. USPN 7,022,342, in view of Sriwongjanya et al. WO 99/61005.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer

in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Chen is relied upon for the reason stated above. Chen does not teach the channeling agent in the controlled release coating layer.

Sriwongjanya teaches a controlled release oral dosage in the form of tablet or pellet comprising an active core, and a controlled release coating layer comprising channeling agent such as methacrylic acid copolymer (page 8, lines 5-19). The dosage form further comprises an immediate release tablet or pellet containing active drug. The controlled release and immediate release tablets or pellets are placed in a hard gelatin capsule for administration to animal or human (page 5, lines 4-10; and page 10, lines 6-9). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the controlled release dosage of Chen to include the immediate release dosage form and the channeling agent in view of the teachings of Sriwongjanya, because Sriwongjanya teaches channeling agent increases the volume of fluid imbibed into the core and creates channels to enable the dosage form to dispense the drug (page 8, lines 7-9), because Sriwongjanya teaches a controlled release dosage form that is easy to manufacture and can be used to prepare a range of dosing levels, because Sriwongjanya teaches a controlled release dosage form having similar C_{max} value and release profile as desired by Chen (page 3, lines 21-27), and because Chen teaches the desirability to obtain a controlled release dosage form characterized by a high extent of absorption, and a high bioavailability that can provide

therapeutic levels of the drug to a subject in need of such treatment over a twelve to twenty-four hour period (column 2, lines 59-67).

Claims 7, 10, 11, 14-16, 24-26, 49, 55, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. USPN 7,022,342, in view of Patel et al. US 6,569,463.

Chen is relied upon for the reasons stated above. Chen does not teach the claimed surfactant in the core composition.

Patel teaches a solid pharmaceutical composition comprising a solid carrier including a substrate and an encapsulation coat comprising active drugs and surfactants (abstract). Surfactant includes tween 80 (polysorbate 80) (tablet 11 at column 19, line 12). The substrate includes pellet, bead, or the like such as sugar or microcrystalline cellulose (column 28, lines 20-40). The solid carrier is further coated with a delayed release coating comprising an enteric polymer, plasticizer, and surfactant (column 34, lines 38-50; and column 35, lines 1-67). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the controlled release dosage of Chen to include the surfactant in view of the teaching of Patel, because Patel teaches using surfactant to increase solubility, improve dissolution, enhance absorption and bioavailability of the active ingredient in the solid carrier (column 9, lines 63 through column 10, lines 1-17), because Patel teaches a dosage form suitable for metoprolol (column 8, line 31), and because Chen teaches the

desirability to obtain a controlled release dosage form characterized by a high extent of absorption, and a high bioavailability (column 2, lines 59-67).

It is noted that the cited references do not explicitly teach the claimed inert core diameter of about 60-80 mesh. However, it would have been obvious to one of ordinary skill in the art to, by routine experimentation optimize the inert core size to obtain the claimed invention, because Chen teaches an inert core having size of about 50 mesh, and because Patel teaches any pharmaceutically known inert core.

Claims 1, 3-9, 14-49, 51-57 and 60-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stark et al. US 6,733,789, in view of Buseti et al. US 6,190,692 and Sriwongjanya et al. WO 99/61005.

Stark teaches a multiparticulate formulation comprising an inert core coated with active drug in the presence of binder and other additives (column 3, lines 45-56). The coated core is further coated with a polymeric coating layer comprising combination/mixture of water-insoluble polymer including cellulose acetate butyrate (column 3, lines 58 through column 4, lines 1-9). The polymeric coating layer further comprises methacrylic acid copolymer (column 4, lines 54-63), one or more soluble excipients including polysorbate, poloxamers, and plasticizer (column 5, lines 54 through column 6, lines 1-36). Stark also teaches the claimed release profile, wherein 0-10% of the active agent is released after 2 hours, less than 50% is released after 4 hours, and greater than 20% is released after 10 hours (column 3, lines 1-20; and table 1). Stark further teaches the multiparticulate can be formulated into tablet or capsule for

oral administration (column 7, lines 4-14). The process for preparing the multiparticulate is disclosed in column 3, lines 45-56; column 6, lines 43-56; and examples).

Stark does not specifically teach the claimed combination of polymers, which include the claimed channeling agent.

Sriwongjanya teaches a controlled release oral dosage in the form of tablet or pellet comprising an active core, and a controlled release coating layer comprising channeling agent such as methacrylic acid copolymer (page 8, lines 5-19). The dosage form further comprises an immediate release tablet or pellet containing active drug. The controlled release and immediate release tablets or pellets are placed in a hard gelatin capsule for administration to animal or human (page 5, lines 4-10; and page 10, lines 6-9). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the controlled release dosage of Stark to include the channeling agent in view of the teachings of Sriwongjanya, because Sriwongjanya teaches channeling agent to increase the volume of fluid imbibed into the core and create channels to enable the dosage form to dispense the drug (page 8, lines 7-9), because Sriwongjanya teaches a controlled release dosage form that is easy to manufacture and can be used to prepare a range of dosing levels, and because Stark teaches combination of polymers in the controlled release coating layer.

Stark does not expressly teach the claimed active drug.

Buseti teaches a controlled release formulation comprising drug includes β -blocker such as bisoprolol and metoprolol succinate (column 4, lines 40-46). Thus, it

would have been obvious to one of ordinary skill in the art to prepare a multiparticulate formulation according to Stark to deliver metoprolol, because Buseti teaches β -blocker such as metoprolol is known in the art, because Buseti teaches the equivalency between bisoprolol and metoprolol, and because Stark teaches a formulation suitable for the delivery of β -blocker active agents.

It is noted that Stark does not explicitly teach the claimed inert core diameter of about 60-80 mesh. However, it would have been obvious to one of ordinary skill in the art to, by routine experimentation optimize the inert core size to obtain the claimed invention, because Stark teaches the use of any pharmaceutically known inert core having size ranges from 0.4-1.1 mm (column 3, lines 42-44).

Claims 10-16, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stark et al. US 6,733,789, in view of Buseti et al. US 6,190,692 and Patel et al. US 6,569,463.

Stark is relied upon for the reason stated above. Stark does not teach the core composed of swellable material such as microcrystalline cellulose.

Patel teaches a solid pharmaceutical composition comprising a solid substrate encapsulated with active drugs and surfactants (abstract). Surfactant includes tween 80 (polysorbate 80) (tablet 11 at column 19, line 12). The substrate includes nonpareil or microcrystalline cellulose (column 28, lines 20-40). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to select microcrystalline cellulose as an inert carrier in view of the teaching of Patel, because

Patel teaches nonpareil seed and microcrystalline cellulose core are well known in pharmaceutical art as an inert carrier, and because Stark teaches the use of any known inert carrier.

Response to Arguments

Applicant's arguments filed 12/18/06 have been fully considered but they are not persuasive.

Applicant indicates that Chen reference is not qualify as prior art because it is owned by the same entity as the present application.

However, in order to be disqualified as prior art under 35 U.S.C. 103(c), the subject matter which would otherwise be prior art to the claimed invention and the claimed invention must be commonly owned, or subject to an obligation of assignment to a same person, at the time the claimed invention was made. See MPEP § 706.02(I) for 35 U.S.C. There must be a statement that the common ownership was "at the time the invention was made."

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1615

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

A handwritten signature in black ink, appearing to read 'S. Tran', is written over the printed name and title.

S. Tran
Patent Examiner
Art Unit 1615

Product: Metoprolol Succinate Active Pellets II

Product Code #: S816 Batch Size: 13.139 kg

Description: White to off-white pellets

Issued By: [Signature]

REDACTED

Date: _____

Item No.	Ingredients	Weight %	Material Code #	Material Rec.#	Amount per Batch (kg)	Expiration Date	Weighted by	Checked by	Date
1.	Metoprolol Succinate Active Pellets I	43.99	S815	202005	5.78			<u>[Signature]</u>	<u>01/13</u>
2.	Metoprolol Succinate, USP	53.28	1059	0110193	7.00			<u>[Signature]</u>	<u>01/13</u>
3.	Hydroxypropyl Methylcellulose, USP (Methocel E-5)	2.66	2116	0110990	0.35			<u>[Signature]</u>	<u>01/13</u>
4.	Polysorbate 80, NF (Tween 80)	0.68	2064	0112074	0.009			<u>[Signature]</u>	<u>01/13</u>
5.	Purified Water, USP	*	2014	01012044	21.00			<u>[Signature]</u>	<u>01/13</u>

Total

100.00

13.139 kg

*Evaporated during processing.

mcpS816.001

Legal

[Signature]

REDACTED

COPY

Formula Approval		Batch Approval	
Prepared by: <u>[Signature]</u>	Date: <u>01/13</u>	Reviewed by: <u>[Signature]</u>	Date: <u>01/13</u>
Reviewed by: <u>[Signature]</u>	Date: <u>01/13</u>	Approved by: <u>[Signature]</u>	Date: <u>01/13</u>

? Cassiope - P

? Pollo - CB

Davidu Garcia - EG

Donna Bracewell - DB

Yzabel Joseph - CY

ISHOMUA BARRETT - LB

Isaiah Soler - RS

RUBEN L. RIVERA - FR

MONGKOL SRIWONGJANYA - MS

Product: Metoprolol Succinate Active Pellets II

Revision #: 001

Product Code #: S816

Batch Size: 13139 kg

Lot #: PD2015

Raw Material Weighing Record

By: Ck'd Date

Step #1

Check to ensure that the area, utensils and equipment have been cleaned. Check and complete the room log book.

Room #: 103

C CB

Step #2

Check all ingredients listed on page # 1 that will be used in the manufacturing process for name, receiving #, raw material code #, and expiration date.

C CB REDACTED

Step #3

Weigh all ingredients and document on the "Raw Material Weighing Record" (page 3). Also document on the "Master Formula" page (page 1).

C CB

Formula Approval

Prepared by: syl

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

WEIGHING LABEL

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/ADrum clean and tare ch'k by: N/A Date: N/A

Product: Purified Water
 Code No.: 2014 Rec/Lot No.: 020220A4
 Gross: 27.820 kg Exp. Date: REDACTED
 Tare: 6.820 kg Whg. By: C
 Net: 21.000 kg Ch'k By: PD
 Scale: 5-109 Date: REDACTED

Product: Metoprolol Succ. Rel. Pellets I
 Code No.: 5815 Rec/Lot No.: P02005
 Gross: 6.84 kg Exp. Date: N/A
 Tare: 1.06 kg Whg. By: C
 Net: 5.78 kg Ch'k By: PD
 Scale: 5-112 Date: REDACTED

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Metoprolol ES
 Code No.: 2116 Rec/Lot No.: 0211624
 Gross: 0.359 kg Exp. Date: REDACTED
 Tare: 0.009 kg Whg. By: C
 Net: 0.350 kg Ch'k By: PD
 Scale: 5-109 Date: REDACTED

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Tween 80
 Code No.: 2064 Rec/Lot No.: 0012074
 Gross: 0.024 kg Exp. Date: REDACTED
 Tare: 0.015 kg Whg. By: C
 Net: 0.009 kg Ch'k By: PD
 Scale: 5-112 Date: REDACTED

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Metoprolol Succ. USP
 Code No.: 1059 Rec/Lot No.: 0110193
 Gross: 10.500 kg Exp. Date: REDACTED
 Tare: 3.500 kg Whg. By: C
 Net: 7.000 kg Ch'k By: PD
 Scale: 5-109 Date: REDACTED

REDACTED

Product: Metoprolol Succinate Active Pellets II

Revision #: 001

Product Code #: S816

Batch Size: 13139 kg

Lot #: PO2013

Raw Material Weighing Record

Item #: 1

Name: Metoprolol Succinate Active Pellets I

Code #: S815

Receiving #: PC2005

Scale #: 5-109

Gross: 6.245 kg

Tare: 1.000 kg

Net: 5.245 kg

Weighed by: [Signature]

Date: [Signature]

Checked by: [Signature]

REDACTED

Item #: 2

Name: Metoprolol Succinate, USP

RM Code #: 1059

Receiving #: 0110193

Scale #: 5-109

Gross: 10.500 kg

Tare: 3.500 kg

Net: 7.000 kg

Weighed by: [Signature]

Date: [Signature]

Checked by: [Signature]

REDACTED

Item #: 3

Name: Hydroxypropyl Methylcellulose, USP (Methocel E-5)

RM Code #: 2116

Receiving #: 0011090

Scale #: 5-112

Gross: 0.259 kg

Tare: 0.009 kg

Net: 0.250 kg

Weighed by: [Signature]

Date: [Signature]

Checked by: [Signature]

REDACTED

Item #: 4

Name: Polysorbate 80, NF (Tween 80)

RM Code #: 2064

Receiving #: 0012074

Scale #: 5-112

Gross: 0.224 kg

Tare: 0.015 kg

Net: 0.209 kg

Weighed by: [Signature]

Date: [Signature]

Checked by: [Signature]

REDACTED

Item #: 5

Name: Purified Water, USP

RM Code #: 2014

Receiving #: 020220A

Scale #: 5-112

Gross: 27.820 kg

Tare: 6.620 kg

Net: 21.200 kg

Weighed by: [Signature]

Date: [Signature]

Checked by: [Signature]

REDACTED

Item #: [Blank]

Name: [Blank]

RM Code #: [Blank]

Receiving #: [Blank]

Scale #: [Blank]

Gross: [Blank] kg

Tare: [Blank] kg

Net: [Blank] kg

Weighed by: [Blank]

Date: [Blank]

Checked by: [Blank]

REDACTED

Item #: [Blank]

Name: [Blank]

RM Code #: [Blank]

Receiving #: [Blank]

Scale #: [Blank]

Gross: [Blank] kg

Tare: [Blank] kg

Net: [Blank] kg

Weighed by: [Blank]

Date: [Blank]

Checked by: [Blank]

REDACTED

Item #: [Blank]

Name: [Blank]

RM Code #: [Blank]

Receiving #: [Blank]

Scale #: [Blank]

Gross: [Blank] kg

Tare: [Blank] kg

Net: [Blank] kg

Weighed by: [Blank]

Date: [Blank]

Checked by: [Blank]

REDACTED

Formula Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: [Blank]

Date: [Blank]

Date: [Blank]

REDACTED

REDACTED

REDACTED

Product: Metoprolol Succinate Active Pellets II

Revision #: 001

Product Code #: S816

Batch Size: 13.13g

Lot #: PD2013

Procedure

By Ck'd Date

Step #4

Check room and equipment for cleanliness, mechanical set-up and proper labeling.
Complete room and equipment log books.

Room #: 117

Equipment #: F-164

EG AN

REDACTED

Step #5

Check containers of all ingredients against formula page for name, receiving #, raw material code #, and amount. Check the weight of all ingredients.

Scale #: S-183

EG MS

Step #6

Dissolve Hydroxypropyl Methylcellulose E-5, USP (Item #3) into Purified Water, USP (Item #5) by using a mechanical stirrer until a clear solution is obtained.

Model: 100-WCC-12

Equipment #: F-144

Start: 10:03 pm

Stop: 11:03 pm

Total Mixing Time: 1 hr

EG MS

REDACTED

Step #7

Add Metoprolol Succinate, USP (Item #2) and Polysorbate 80, NF (Tween 80) (Item #4) into solution from Step #6 by using a mechanical stirrer.

Model: 100-WCC-12

Equipment #: F-144

Start: 11:12 pm

Stop: 11:42 pm

Total Mixing Time: 30 min

EG MS

REDACTED

Formula Approval

Prepared by: Syuk

Reviewed by: [Signature]

Approved by: L. Suage

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol Succinate Active Pellets II

Revision #: 001

Product Code #: S816 Batch Size: 13.139 kg

Lot #: P02013

Procedure

By _____ Ck'd _____ Date _____

Step #8

Continue stirring the suspension from Step #7 until it is completely consumed in Step #12.

EG ✓

Step #9

Use the following guidelines to set up the bottom spray fluidized bed coater:

Model #: GPCG-15 Equipment #: F-164

- | | |
|-----------------------------|-----------------|
| a) Nozzle height: | <u>Bottom</u> |
| b) Nozzle tip: | <u>1.2 mm</u> |
| c) Screen size: | <u>100 mesh</u> |
| d) Shaking interval: | <u>30 min</u> |
| e) Shaking duration: | <u>3 sec</u> |
| f) Atomization pressure: | <u>2.5</u> |
| g) Inlet air temperature: | <u>71</u> |
| h) Pump rate: | <u>10 ml</u> |
| i) Tubing size: | <u>16 mm</u> |
| j) Regulation flap setting: | <u>1/4</u> |
| k) Center Column: | <u>40 mm</u> |

The above parameters should be utilized only as guidelines.

EG ✓ REDACTED

Step #10

Set inlet air temperature at 50-100°C. Make sure product or outlet air temperature is higher than 45°C prior to loading the Metoprolol Succinate Active Pellets I (Item #1) into fluidized product bowl.

EG ✓

Step #11

Charge Metoprolol Succinate Active Pellets I (Item #1) into the fluidized bed product bowl.

EG ✓ REDACTED

Formula Approval

Prepared by: synReviewed by: [Signature]Approved by: [Signature]Date: REDACTEDDate: REDACTEDDate: REDACTED

Product: Metoprolol Succinate Active Pellets II

Revision #: 001

Product Code #: S816

Batch Size: 13.139 kg

Lot #: P02013

Procedure

Step #12

Initiate drug-layering cycle employing the parameters in Step #9 as a guideline and spray the suspension from Step #7 onto the substrate.

By _____ Ck'd _____ Date: _____

EG RS

Step #13

After completion of the process, dry the pellets for 5 minutes or until the LOD is less than 3%. Record the drying information on the In-Process Data Sheet

Moisture balance model: JCCOYL

Equipment #: F-190

Sample Weight: 4.557 g

Final LOD: 0.313 %

Start Drying: 11:44

Stop Drying: 11:49

Total Drying Time: 5 min

Note: All In-Process Data Sheets to be filed with the batch record.

Step #14

Discharge the dried pellets into a properly identified container lined with double polyethylene bags and record weight.

Scale #: S-183

Gross: 13.54 kg

Tare: 1.07 kg

Net: 12.46 kg

Formula Approval

Prepared by: Sybil

Reviewed by: [Signature]

Approved by: L. Savage

Date: REDACTED

Date:

REDACTED

Date:

REDACTED

Andrx Pharmaceuticals, Inc.

Revision #: 001

Product: Metoprolol Succinate Active Pellets II

Product Code #: S816 Batch Size: 13.135 kg Lot #: P03013

By Ck'd Date

Step #15

Screen the pellets from Step #14 on 35 mesh and 60 mesh.
 Collect the pellets between 35 and 60 mesh. Remove approximately
 0.02 kg sample for QC testing.

Scale #: S-194 Gross QC Weight: 0.04 kg
 Tare Weight: 0.02 kg
 Net QC sample Weight: 0.02 kg

PS IB REDACTEDStep #16

Record the weight of acceptable Pellets from Step #15.

Scale #: S-183

Gross: 12.98 kg
 Tare: 1.08 kg
 Net: 11.90 kg

DB 2 REDACTEDStep #17 - Batch Accountability-Active Layering

- (a) Sample weight for % LOD analysis (Step #13) 0.004 kg
 (b) Sample weight for QC testing (Step #15) 0.020 kg
 (c) Weight of acceptable pellets (Step #16) 11.90 kg
 (d) Weight of all in-process rejects: 1.048 kg
 (e) Actual yield (a+b+c+d): 12.952 kg
 (f) Theoretical yield: 13.135 kg
 (g) Percent accountable for (e/f x 100): 98.7 98.6 LC %

REC DB REDACTED

Formula Approval

Prepared by: Suh Reviewed by: [Signature] Approved by: [Signature]
 Date: REDACTED Date: REDACTED Date: REDACTED

Product: Metoprolol Succinate Active Pellets II Product Code: S816

Batch Size: 13.139 kg Lot #: 022013

Equipment Set-Up:

Machine Model #: GNC-15

Pump Model #: AccustepEx

Column Height: 40mm

Equipment #: F-1164

Equipment #: F-126

Nozzle Size: 1.2mm

Insert Type: Water

Plate Type: B

Shaking Interval: 30min

Size: 9"

Inlet Air Regulation Flap: 1/4

Shaking time: 3.5s

Comments:

REDACTED

Date:

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
12:05pm	10.0	0.00	170.74	16.12	2.5	46.24	50.51	69.19	207.56	9.80	EG	start spray
12:20pm	12.0	0.16	170.55	32.23	2.5	45.31	49.56	61.04	229.43	10.38	EG	
12:35pm	14.0	0.36	171.52	51.40	2.5	45.51	51.10	66.11	220.99	9.80	EG	
12:50pm	16.0	0.56	172.31	53.35	2.5	45.19	50.27	64.48	232.22	10.31	DB	
1:05pm	18.0	0.80	174.45	61.46	2.5	44.75	49.80	65.26	209.27	9.87	DB	
1:20pm	20.0	1.08	171.33	64.71	2.5	44.96	49.39	65.80	219.30	10.14	EG	
1:35pm	22.0	1.36	176.41	78.94	2.5	44.42	49.40	67.41	214.64	10.24	EG	
1:50pm	24.0	1.68	180.71	91.19	2.5	44.58	49.68	68.19	219.28	9.83	EG	
2:05pm	26.0	2.06	179.14	89.12	2.5	44.76	49.49	69.90	216.59	9.83	EG	
2:20pm	28.0	2.46	180.12	84.44	2.5	44.46	49.56	70.00	213.42	9.80	EG	
2:35pm	30.0	2.88	174.26	98.89	2.5	43.87	49.12	64.57	217.31	9.91	EG	
2:50pm	32.0	3.34	183.65	99.55	2.5	43.60	48.41	70.04	223.67	9.85	EG	
3:05pm	34.0	3.82	188.33	112.07	2.5	43.27	49.66	74.71	219.55	10.14	EG	
3:20pm	36.0	4.34	185.00	103.41	2.5	44.31	50.07	75.39	212.93	9.94	EG	

REDACTED

Formal Approval

Approved by: *[Signature]*

Date: REDACTED

Reviewed by: *[Signature]*

Date: REDACTED

Prepared by: *[Signature]*

Date: REDACTED

Product: Metoprolol Succinate Active Pellets II

Product Code: S816

Batch Size: 13.139 kg

Lot #: 203013

~~REDACTED~~

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
3.15m	38.0	4.90	181.10	117.93	2.5	44.24	50.00	76.73	221.23	9.73	EG	
3.50m	40.0	5.48	194.19	120.50	2.5	44.09	49.78	76.98	216.10	10.07	DB	
4.05m	42.0	6.08	191.26	130.14	2.5	43.87	49.24	76.81	221.72	12.74	DB	
4.20m	44.0	6.72	201.22	138.93	2.5	43.53	48.78	77.00	208.78	10.07	DB	
4.35m	46.0	7.40	211.96	151.61	2.5	43.12	48.00	78.42	220.58	9.87	DB	
4.50m	48.0	8.10	191.94	140.40	2.5	42.80	48.22	79.98	211.72	10.11	DB	
5.05m	50.0	8.82	196.53	161.40	2.5	43.36	49.44	82.01	241.50	10.07	EG	
5.35m	50.0	10.34	203.86	162.13	2.5	44.48	50.56	82.40	246.36	9.94	DB	
6.05m	50.0	11.86	219.78	200.71	2.5	44.78	50.90	83.46	243.94	9.77	DB	
6.35m	50.0	13.38	220.17	217.68	2.5	44.80	50.81	83.03	237.35	10.14	DB	
7.05m	50.0	14.58	237.01	230.62	2.5	45.12	51.29	82.71	234.91	10.24	DB	
7.35m	50.0	16.54	238.34	244.54	2.5	45.12	51.27	82.96	241.50	10.14	DB	
8.05m	50.0	17.70	225.44	244.66	2.5	43.55	48.07	77.25	215.62	10.11	DB	
8.35m	50.0	17.22	233.41	290.60	2.5	43.75	49.61	81.67	229.78	10.21	DB	
9.05m	50.0	20.72	244.77	302.45	2.5	43.97	49.23	82.06	232.13	10.04	DB	
9.35m	50.0	22.28	243.81	321.57	2.5	44.09	49.90	81.91	228.31	10.00	DB	
10.05m	50.0	23.80	240.43	335.74	2.5	44.31	50.17	81.96	227.34	9.94	DB	
10.50m	50.0	25.26	257.04	354.41	2.5	44.53	50.34	91.71	231.97	10.00	DB	

Formula Approval

Prepared by: Syn

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

In-Process Data Sheet

Batch Size 13.134 Lot #: 12

Product Code:S816

Product: Metoprolol Succinate Active Pellets II

Date: REDACTED

[illegible]

Formula Approval //

Reviewed by: Subh Approved by: D. J. D. J. D. J. D. J.

Prepared by: Date: REDACTED =

Product: Metoprolol Succinate Active Pellets I

Product Code #: S815 Batch Size: 14.862 kg Lot #: 202005

Description: White to off-white pellets

REDACTED

Issued By: [Signature] Date:

Item #	Ingredients	Weight %	Material Code #	Material Lot #/Rec. #	Amount per batch (kg)	Expiration Date	Weighted by	Checked by	Date
1.	Sugar Spheres, NF (60/80)	36.33	2084	0611078	5.40			<u>EB</u>	
2.	Metoprolol Succinate, USP	60.56	1059	0110193	9.0			<u>EB</u>	
3.	Hydroxypropyl Methylcellulose, USP (Methocel E-5)	3.03	2116	9903005	0.45			<u>EB</u>	
4.	Polysorbate 80, NF (Tween 80)	0.08	2064	0011674	27.0			<u>EB</u>	
5.	Purified Water, USP	*	2014	0611601	0.812			<u>EB</u>	

Total

100.00

*Evaporated during processing.

14.862 kg

COPY


Legal [Signature] REDACTED

mcpS815.001

Formula Approval		Batch Approval	
Prepared by: <u>[Signature]</u>	Date: <u> </u>	Reviewed by: <u>[Signature]</u>	Date: <u> </u>
Reviewed by: <u>[Signature]</u>	Date: <u> </u>	Approved by: <u> </u>	Date: <u> </u>
Approved by: <u>[Signature]</u>	Date: <u> </u>		

R. Cassola - P

Q. Sello - CS

 - EG

Cathy Hunter - CH

P. Ben D. Rivera - PR

Roger Cooke - RC

MONGKOL SRINONGYANYA - MS

Product: Metoprolol Succinate Active Pellets I

Revision #: 001

Product Code #: S815

Batch Size: 14.862 kg

Lot #: R02005

Raw Material Weighing Record

By Ck'd Date

Step #1

Check to ensure that the area, utensils and equipment have been cleaned. Check and complete the room log book.

Room #: 103

REDACTED

P CP

Step #2

Check all ingredients listed on page # 1 that will be used in the manufacturing process for name, receiving #, raw material code #, and expiration date.

REDACTED

P CP

Step #3

Weigh all ingredients and document on the "Raw Material Weighing Record" (page 3). Also document on the "Master Formula" page (page 1).

REDACTED

P CP

Formula Approval

Prepared by: Sph

Reviewed by: [Signature]

Approved by: [Signature]

Date:

Date:

Date:

REDACTED

REDACTED

REDACTED

Product: Metoprolol Succinate Active Pellets I

Revision #: 001

Product Code #: S815

Batch Size: 14.562 kg

Lot #: P02005

Raw Material Weighing Record

Item #: 1

Name: Sugar Spheres, NF (60/80)

RM Code#: 2084

Receiving #: 0011072

Scale #: 5-112

Gross: 5.438 kg

Tare: 0.038 kg

Net: 5.400 kg

Weighed by: [Signature]

Date: [Redacted]
Checked by: [Signature]

Item #: 2

Name: Metoprolol Succinate, USP

RM Code#: 1059

Receiving #: 0110193

Scale #: 5-109

Gross: 9.095 kg

Tare: 0.095 kg

Net: 9.000 kg

Weighed by: [Signature]

Date: [Redacted]
Checked by: [Signature]

Item #: 3

Name: Hydroxypropyl Methylcellulose, USP (Methocel E-5)

RM Code#: 2116

Receiving #: 9903005

Scale #: 5-112

Gross: 0.458 kg

Tare: 0.008 kg

Net: 0.450 kg

Weighed by: [Signature]

Date: [Redacted]
Checked by: [Signature]

Item #: 4

Name: Polysorbate 80, NF (Tween 80)

RM Code#: 2064

Receiving #: 0012074

Scale #: 5-112

Gross: 0.027 kg

Tare: 0.015 kg

Net: 0.012 kg

Weighed by: [Signature]

Date: [Redacted]
Checked by: [Signature]

Item #: 5

Name: Purified Water, USP

RM Code#: 2014

Receiving #: 020116 API

Scale #: 5-109

Gross: 44.364 kg

Tare: 17.364 kg

Net: 27.000 kg

Weighed by: [Signature]

Date: [Redacted]
Checked by: [Signature]

Item #: [Redacted]

Name: [Redacted]

RM Code#: [Redacted]

Receiving #: [Redacted]

Scale #: [Redacted]

Gross: [Redacted] kg

Tare: [Redacted] kg

Net: [Redacted] kg

Weighed by: [Redacted]

Date: [Redacted]
Checked by: [Redacted]

Item #: [Redacted]

Name: [Redacted]

RM Code#: [Redacted]

Receiving #: [Redacted]

Scale #: [Redacted]

Gross: [Redacted] kg

Tare: [Redacted] kg

Net: [Redacted] kg

Weighed by: [Redacted]

Date: [Redacted]
Checked by: [Redacted]

Item #: [Redacted]

Name: [Redacted]

RM Code#: [Redacted]

Receiving #: [Redacted]

Scale #: [Redacted]

Gross: [Redacted] kg

Tare: [Redacted] kg

Net: [Redacted] kg

Weighed by: [Redacted]

Date: [Redacted]
Checked by: [Redacted]

Formula Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: [Redacted]

Date: [Redacted]

Date: [Redacted]

Product: Metoprolol Succinate Active Pellets I

Revision #: 001

Product Code #: S815 Batch Size: 14.262 kg Lot #: 202005

Procedure

By Ck'd Date

Step #4

✓
Check room and equipment for cleanliness, mechanical set-up and proper labeling.
Complete room and equipment log books.

Room #: 117

Equipment #: F-144

CH EG REDACTED

Step #5

Check containers of all ingredients against formula page for name, receiving #, raw material code #, and amount. Check the weight of all ingredients.

Scale #: 5.184

CH EG REDACTED

Step #6

Dissolve Hydroxypropyl Methylcellulose, USP (E-5) (Item #3) into Purified Water, USP (Item #5), by using a mechanical stirrer until a clear solution is obtained.

Model: 1A1-1111A Equipment #: F-199

Start: 8:40pm Stop: 10:20pm

Total Mixing Time: 1 hr and 40 min

EG CH REDACTED

Step #7

Add Metoprolol Succinate, USP (Item #2) and Polysorbate 80, NF (Tween 80) (Item #4) into solution from Step #6 by using a mechanical stirrer.

Model: 1A1-1111A Equipment #: F-199

Start: 10:30pm Stop: 11:10pm

Total Mixing Time: 40 min

EG CH REDACTED

Formula Approval

Prepared by: Sph Reviewed by: [Signature] Approved by: [Signature]

Date: REDACTED Date: REDACTED Date: REDACTED

Product: Metoprolol Succinate Active Pellets I

Revision #: 001

Product Code #: S815 Batch Size: 14.862 kg

Lot #: 402005

Procedure

By Ck'd Date

Step #8

Continue stirring the suspension from Step #7 until it is completely consumed in Step #12.

EG CH REDACTED

Step #9

Use the following guidelines to set up the bottom spray fluidized bed coater:

Model #: GPCG-15 Equipment #: F-164

- | | |
|-----------------------------|-----------|
| a) Nozzle height: | Bottom |
| b) Nozzle tip: | 1.2 mm |
| c) Screen size: | 100 mesh |
| d) Shaking interval: | 30 min |
| e) Shaking duration: | 3 sec |
| f) Atomization pressure: | 2.5 bar |
| g) Inlet air temperature: | 50-100 °C |
| h) Pump rate: | 5 ml/min |
| i) Tubing size: | 16 mm |
| j) Regulation flap setting: | 1/4 |
| k) Center Column: | 40 mm |

The above parameters should be utilized only as guidelines.

EG CH REDACTED

Step #10

Set inlet air temperature at 50-100°C. Make sure product or outlet air temperature is higher than 45°C prior to loading the sugar spheres, NF (60/80) (Item #1) into fluidized product bowl.

EG CH REDACTED

Step #11

Charge Sugar Spheres, NF (60/80) (Item #1) into the fluidized bed product bowl.

EG CH REDACTED

Formula Approval

Prepared by: syh Reviewed by: [Signature] Approved by: [Signature]

Date: REDACTED Date: REDACTED Date: REDACTED

Product: Metoprolol Succinate Active Pellets I

Revision #: 001

Product Code #: S815 Batch Size: 14.862 kg Lot #: P02005

Procedure

Step #12

Initiate drug-layering cycle employing the parameters in Step #9 as a guideline and spray the suspension from Step #7 onto the substrate.

By Ck'd Date

EC RSC

REDACTED

Step #13

After completion of the process, dry the pellets for 5 minutes or until the LOD is less than 3%. Record the drying information on the In-Process Data Sheet.

Moisture balance model: Computrac Equipment #: F-190

Sample Weight: 3,939.6 g Final LOD: 0.371 %

Start Drying: 4:55 PM Stop Drying: 5:10 PM

Total Drying Time: 15 min

RSC RSC

REDACTED

Note: All In-Process Data Sheets to be filed with the batch record.

Step #14

Discharge the dried pellets into a properly identified container lined with double polyethylene bags and record weight.

Scale #: S-184

Gross: 14.11 kg

Tare: 1.08 kg

Net: 13.03 kg

RSC RSC

REDACTED

Formula Approval

Prepared by: [Signature] Reviewed by: [Signature] Approved by: F. Savage

Date: [Signature] Date: [Signature] Date: [Signature]

REDACTED

REDACTED

Product: Metoprolol Succinate Active Pellets I

Revision #: 001

Product Code #: S815 Batch Size: 14.862 kg Lot #: 702005

By Ck'd Date

Step #15

Screen the pellets from Step #14 on 40 mesh and 60 mesh.
Collect the pellets between 40 and 60 mesh. Remove approximately
0.02 kg sample for QC testing.

Scale #: S-194 Gross QC Weight: 0.040 kg
Tare Weight: 0.020 kg
Net QC sample Weight 0.020 kg

Rec ra REDACTEDStep #16

Record the weight of acceptable Pellets from Step #15.

Scale #: S-184

Gross: 11.92 kg
Tare: 0.040 kg
Net: 11.88 kg

Rec ra REDACTEDStep #17 - Batch Accountability-Active Layering

(a) Sample weight for % LOD
analysis (Step #13) 0.004 kg
(b) Sample weight for QC testing
(Step #15) 0.020 kg
(c) Weight of acceptable pellets
(Step #16) 11.88 kg
(d) Weight of all in-process rejects: 2.541 kg
(e) Actual yield (a+b+c+d): 14.445 kg
(f) Theoretical yield: 14.862 kg
(g) Percent accountable for
(e/f x 100): 97.2 %

Rec ra REDACTED

Formula Approval

Prepared by: SJA Reviewed by: [Signature] Approved by: X. Savage
Date: [Redacted] Date: [Redacted] Date: [Redacted]

In-Process Data Sheet

Revision #: 001

Product: Metoprolol Succinate Active Pellets I Product Code: S815

Batch Size: 14.862 kg Lot #: 22005

Equipment Set-Up:

Machine Model #: GPC-15

Equipment #: F-164

Insert Type: 2252426

Size: 4"

Pump Model #: Masterflex

Equipment #: F-126

Plate Type: B Tube Size: 16mm Inlet Air Regulation Flap: 100%

Column Height: 43mm

Nozzle Size: 12mm

Shaking Interval: 30min

Shaking time: 3 sec

Comments:

Date: REDACTED

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
12:25.0	5.0	0.00	165.66	18.07	2.5	40.65	50.29	69.85	245.90	9.54	EG	Start
12:40.0	6.0	0.03	188.72	63.12	2.5	42.90	49.78	57.64	249.31	9.90	EG	
12:55.0	7.0	0.18	172.11	69.22	2.5	42.65	49.56	59.77	249.56	9.56	EG	
1:10.0	8.0	0.28	175.43	70.14	2.5	43.19	49.76	60.12	247.61	9.73	EG	
1:25.0	9.0	0.40	176.60	81.68	2.5	43.53	50.54	62.47	247.36	11.87	EG	
1:40.0	10.0	0.54	177.48	78.79	2.5	43.55	49.95	61.45	250.54	10.11	CH	
1:55.0	11.0	0.70	175.41	89.60	2.5	43.46	49.51	61.66	251.27	10.31	CH	
2:10.0	11.0	0.86	174.45	82.04	2.5	43.36	49.17	60.91	249.07	10.11	CH	
2:25.0	13.0	1.04	185.78	97.55	2.5	43.80	50.00	62.21	250.40	11.66	EG	
2:40.0	14.0	1.22	188.51	96.20	2.5	44.31	49.69	60.86	254.44	10.68	EG	
2:55.0	15.0	1.42	169.18	104.14	2.5	43.82	49.73	62.60	248.58	9.97	EG	
3:10.0	16.0	1.66	173.48	121.11	2.5	43.41	49.12	62.38	250.40	10.11	EG	
3:25.0	17.0	1.90	180.71	115.25	2.5	44.02	50.27	64.62	253.95	9.87	EG	

Formula Approval

Prepared by: Sybil

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol Succinate Active Pellets I

Product Code: S815

Batch Size: 14,862 kg Lot #: 202055

~~REDACTED~~

Date:

Time	Pump Rate Reading (ml/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
3:45m	18.0	2.10	172.70	96.51	2.5	43.51	48.08	61.38	255.41	9.77	EG	
3:55m	19.0	2.38	178.36	134.66	2.5	42.90	48.34	62.00	244.67	10.45	EG	
4:05m	20.0	2.66	184.42	137.47	2.5	42.67	48.76	62.33	254.93	9.90	EG	
4:15m	22.0	2.96	184.01	127.95	2.5	42.63	48.24	62.09	256.15	10.24	CH	
4:25m	21.0	3.36	182.46	137.10	2.5	42.41	47.88	62.94	251.56	10.18	CH	
4:35m	24.0	3.67	188.91	151.87	2.5	42.14	47.57	63.11	249.80	10.11	CH	
5:05m	26.0	3.98	182.15	156.12	2.5	42.87	47.14	63.16	246.87	10.00	CH	
5:15m	26.0	4.16	191.65	162.01	2.5	42.75	47.22	64.21	248.58	10.18	CH	
5:40m	30.0	4.78	188.91	167.18	2.5	42.45	47.02	64.06	242.97	9.87	CH	
5:55m	32.5	5.16	195.16	185.70	2.5	42.31	48.44	67.82	254.20	9.73	CH	
6:10m	34.0	5.72	194.58	176.90	2.5	42.48	49.16	70.07	253.47	9.46	CH	
6:25m	36.0	6.24	192.90	196.82	2.5	42.47	48.22	68.51	242.72	10.28	CH	
6:40m	38.0	6.50	198.87	190.82	2.5	42.48	48.36	69.80	255.06	10.00	EG	
6:55m	40.0	7.38	203.37	203.76	2.5	42.14	48.00	70.24	246.14	10.21	EG	
7:05m	42.0	7.98	200.14	222.56	2.5	42.29	48.41	72.56	250.54	9.47	EG	
7:25m	44.0	8.02	203.15	215.48	2.5	42.21	48.24	72.61	260.30	9.40	EG	
7:40m	46.0	8.28	204.34	223.54	2.5	42.16	48.19	73.75	252.47	9.66	EG	

Formula Approval

Prepared by: Syah

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol Succinate Active Pellets I

Product Code: S815

Batch Size: 14,862 kg Lot #: 202005

REDACTED

Date:

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
7:55am	49.0	10.00	210.60	233.67	2.5	42.24	48.66	75.83	250.98	9.90	EC	
8:10am	50.0	10.72	209.42	230.13	2.5	42.92	49.27	76.49	235.40	10.24	EC	
8:25am	50.0	11.48	212.16	236.24	2.5	42.85	48.97	76.68	251.51	10.01	EC	
8:40am	50.0	12.26	209.42	254.18	2.5	43.09	49.32	77.17	253.95	9.97	EC	
8:55am	50.0	13.60	221.34	260.41	2.5	43.21	49.41	77.12	248.58	9.80	PRC	
9:10am	50.0	13.76	212.55	261.26	2.5	43.31	49.41	77.15	256.64	9.97	PRC	
9:25am	50.0	14.48	214.47	270.32	2.5	43.33	49.46	77.32	255.17	9.94	EC	
9:40am	50.0	15.26	210.21	275.11	2.5	43.38	49.32	77.15	257.02	9.73	EC	
9:55am	50.0	16.02	217.72	277.24	2.5	43.43	49.37	77.17	246.38	9.97	PRC	
10:10am	50.0	16.78	232.04	295.74	2.5	43.41	49.41	77.05	247.06	10.04	PRC	
10:25am	50.0	17.75	221.15	300.57	2.5	43.43	49.39	77.15	249.56	9.83	PRC	
10:40am	50.0	19.22	235.05	308.88	2.5	43.58	49.44	76.83	253.71	9.94	PRC	
10:55am	50.0	20.82	252.40	334.76	2.5	43.58	49.44	76.81	250.29	10.11	PRC	
11:10am	50.0	22.30	251.23	403.25	2.5	44.24	50.54	76.59	269.58	10.04	PRC	
11:25am	50.0	23.82	262.95	361.12	2.5	43.63	49.10	73.78	263.65	10.14	PRC	
11:40am	50.0	25.38	273.11	341.16	2.5	43.53	49.22	73.97	287.90	9.87	PRC	

REDACTED

Formulator Approval

Approved by: LSavage

Date: REDACTED

Reviewed by: dyll

Date: REDACTED

Prepared by: Sybil

Date: REDACTED

In-Process Data Sheet

Product: Metoprolol Succinate Active Pellets I

Product Code: S815

Batch Size: 14.562 kg Lot #: _____

32

REDACTED

[illegible]

Formula Approval

Approved by: Alvarez

Date RE-DATED _____

Reviewed by:

Date: ~~REDACTED~~

Prepared by:

Date: 11/01/2015

In-Process Data Sheet

Product: Metoprolol Succinate Active Pellets I

Product Code: S815

Batch Size: 14,862 Kg Lot #: _____

#107
Lot #:

DATE

[illegible]

Formula Approval

Reviewed by: Shah
Approved by: Shah

Reviewed by; _____

Approved by: E. L. Lutz

Date: 11/1/80

Date: ~~REDACTED~~ - ~~REDACTED~~ //

Date: 11/16/2010

aProduct: Metoprolol ER Tablets, 200 mg (Uncoated)

Page 1 of 15

Product Code #: S818

Revision #: 002

Batch Size: 1.124 kg

Lot #: 202017

Description: White oval, shaped tablets (0.3430" x 0.6870")

Issued by: [Signature]

Date: REDACTED

MASTER FORMULA

Item #	Ingredients	Weight %	Material Code #	Material Lot #/Rec. #	Amount per batch (kg)	Expiration Date	Weighted by	Checked by	Date
1.	Metoprolol Succinate ER Pellets	<u>36.368</u>	S817	<u>202014</u>	<u>0.409</u>	<u>N/A</u>	<u>MS</u>	<u>gy</u>	<u>REDACTED</u>
2.	Metoprolol Succinate Active Pellets II	<u>5.071</u>	S816	<u>202013</u>	<u>0.057</u>	<u>N/A</u>	<u>MS</u>	<u>gy</u>	<u>REDACTED</u>
3.	Microcrystalline Cellulose, NF (Avicel PH-102)	<u>6.673</u>	2067	<u>202009</u>	<u>0.075</u>		<u>MS</u>	<u>gy</u>	<u>REDACTED</u>
4.	Microcrystalline Cellulose, NF (Avicel PH-200)	<u>26.868</u>	2168	<u>271022</u>	<u>0.302</u>		<u>MS</u>	<u>gy</u>	<u>REDACTED</u>
5.	Glyceryl Monostearate 600P, NF	<u>20.013</u>	2055	<u>2025125</u>	<u>0.225</u>		<u>MS</u>	<u>gy</u>	<u>REDACTED</u>
6.	Crospovidone (XL-10), NF	<u>4.982</u>	2008	<u>202043</u>	<u>0.056</u>		<u>MS</u>	<u>gy</u>	<u>REDACTED</u>
Total		100.0							

Legal: [Signature]

COPY

METS818.002

Formula Approval	Batch Approval
Prepared by: <u>[Signature]</u> Date: <u>REDACTED</u>	Reviewed by: <u>[Signature]</u> Date: <u>REDACTED</u>
Reviewed by: <u>[Signature]</u> Date: <u>REDACTED</u>	Approved by: <u>[Signature]</u> Date: <u>REDACTED</u>

P. Cassola - C

@ Bello - CB

Sam Yuk - Sg

MONGKOL SRIWONGTANYA - MS

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1.124 kg

Lot#: 202019

Raw Material Weighing Record

PRECAUTION: WEAR SUITABLE RESPIRATOR AND DISPOSABLE GLOVES AT ALL TIMES
WHEN HANDLING THE PRODUCT OR RAW MATERIALS.

By Ck'd Date

Step #1

Check the room and all utensils including containers, polyethylene bags, covers, scoops, spatulas, etc. for cleanliness. Complete room log book.

Room #: 103

Step #2

Check all ingredients listed on page # 1 that will be used in the manufacturing process for name, material code#, receiving#, and expiration date.

Step #3

Weigh all ingredients and document on the "Material Weighing Record".

REDACTED

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated).

Revision #: 002

Product Code: S818 Batch Size: 1.124 kg Lot #: P02019

Material Weighing Record

Item #: 1

Name: Metoprolol Succinate ER Pellets

Code#: S817 Lot #: (664) P02014

Scale #: 5-112

Gross: 0.432 kg

Tare: 0.023 kg

Net: 0.409 kg

Weighted by: [Signature]

Checked by: [Signature]

REDACTED

Item #: 2

Name: Metoprolol Succinate Active Pellets II

RM Code#: S816 Receiving #: P01013

Scale #: 5-112

Gross: 0.063 kg

Tare: 0.006 kg

Net: 0.057 kg

Weighted by: [Signature]

Checked by: [Signature]

REDACTED

Item #: 3

Name: Microcrystalline Cellulose, NF (Avicel PH-102)

RM Code#: 2067 Receiving #: P013059

Scale #: 5-112

Gross: 0.081 kg

Tare: 0.006 kg

Net: 0.075 kg

Weighted by: [Signature]

Checked by: [Signature]

REDACTED

Item #: 4

Name: Microcrystalline Cellulose, NF (Avicel PH-200)

RM Code#: 2168 Receiving #: 9711021

Scale #: 5-112

Gross: 0.310 kg

Tare: 0.008 kg

Net: 0.302 kg

Weighted by: [Signature]

Checked by: [Signature]

REDACTED

Item #: 5

Name: Glyceryl Monostearate 600P, NF

RM Code#: 2055 Receiving #: P05105

Scale #: 5-112

Gross: 0.233 kg

Tare: 0.008 kg

Net: 0.225 kg

Weighted by: [Signature]

Checked by: [Signature]

REDACTED

Item #: 6

Name: Crospovidone (XL-10), NF

RM Code#: 2008 Receiving #: 9909043

Scale #: 5-112

Gross: 0.062 kg

Tare: 0.006 kg

Net: 0.056 kg

Weighted by: [Signature]

Checked by: [Signature]

REDACTED

Item #: _____

Name: _____

RM Code#: _____ Receiving #: _____

Scale #: _____

Gross: _____ kg

Tare: _____ kg

Net: _____ kg

Weighted by: _____

Checked by: _____

REDACTED

Item #: _____

Name: _____

RM Code#: _____ Receiving #: _____

Scale #: _____

Gross: _____ kg

Tare: _____ kg

Net: _____ kg

Weighted by: _____

Checked by: _____

REDACTED

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: ALICEL PH-102
Code No.: 2067 Rec/Lot No.: 0103004
Gross: 0.081 kg Exp. Date: REDACTED
Tare: 0.006 kg Whg. By: C
Net: 0.075 kg Ch'k By: CP
Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Tab 200mg (uncoated)
Code No.: 2008 Rec/Lot No.: 9909041

Gross: 0.062 kg Exp. Date: REDACTED
Tare: 0.006 kg Whg. By: C
Net: 0.056 kg Ch'k By: CP
Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Tab 200mg (uncoated)
Product: ALICEL PH-200
Code No.: 2168 Rec/Lot No.: 9711022
Gross: 0.310 kg Exp. Date: REDACTED
Tare: 0.008 kg Whg. By: C
Net: 0.302 kg Ch'k By: CP
Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Tab 200mg (uncoated)
Code No.: 15811 Rec/Lot No.: REDACTED
Gross: 0.432 kg Exp. Date: N/A
Tare: 0.023 kg Whg. By: C
Net: 0.409 kg Ch'k By: CP
Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Tab 200mg (uncoated)
Gross: 0.463 kg Exp. Date: N/A
Tare: 0.006 kg Whg. By: C
Net: 0.057 kg Ch'k By: CP
Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Tab 200mg (uncoated)

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Glycerol Monostearate 600
Code No.: 2065 Rec/Lot No.: 0105105
Gross: 0.233 kg Exp. Date: REDACTED
Tare: 0.008 kg Whg. By: C
Net: 0.225 kg Ch'k By: CP
Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Tab 200mg (uncoated)

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1.124 kg

Lot #: 103019

Blending

By: MS Ck'd: sy Date:

Step #4

Check room and equipment for cleanliness, mechanical set-up and proper labeling.
Complete room and equipment log books.

Room #: III Equipment #: F-009

MS sy

REDACTED

Step #5

Check containers of all ingredients against formula page for name, material code #,
and amount. Check the weight of all the ingredients.

Scale #: S-004

MS sy

REDACTED

Step #6

Charge the following ingredients (Item # 3,4 and 6) into a suitable blender and
mix for 2 minutes.

Microcrystalline Cellulose, NF (Avicel PH-102) (Item #3)

Microcrystalline Cellulose, NF (Avicel PH-200) (Item #4)

Crospovidone (XL-10), NF (Item #6)

Model: LB-7511 Equipment #: F-009 Size: 8 qt Speed: 23 rpm

Time Start: 5:39 PM Time Stop: 5:41 PM Total Blending time: 2 mins MS sy

Step #7

Pass the mixture from Step # 6 through a hand screen (30 mesh size) or a Comil
equipped with a suitable size stainless screen (30 mesh equivalent) into clean, double
polyethylene bags.

Equipment#: N/A

Screen Size: 30 mesh

MS sy

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol Succinate ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1.120 kg

Lot#: 102019

By Ck'd Date

Step #8

Charge the screened mixture from Step #7 into a suitable blender and add Metoprolol Succinate ER Pellets (Item #1) and Metoprolol Succinate Active Pellets II (Item #2) into the blender.

Model: LB-7511 Equipment #: F-009 Size: 8 qt.

MS Sy

REDACTED

Step #9

Blend for fifteen (15) minutes.

Time Start: 5:46 PM Time Stop: 6:01 PM Speed: 23 rpm

Total Blending Time: 15 mins

MS Sy

Step #10

Pass the Glyceryl Monostearate, 600P (Item #5) by hand through a #30 mesh screen and add to the blend in Step #9.

LF/CO MS

REDACTED

Step #11

Blend for ten (10) minutes.

Time Start: 6:02 PM Time Stop: 6:12 PM Speed: 23 rpm

Total Blending Time: 10 mins

MS CO

REDACTED

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date:

Date:

Date:

REDACTED

REDACTED

REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1.124 kg Lot #: 402017

By: Ck'd Date

Step #12

Collect the blend from Step #11 in a clean, tared, properly identified drum lined with double polyethylene bags. Weigh and record the weight of the blend.

Scale: S-004

Gross Weight: 1.144 kg

Tare Weight: 0.012 kg

Net Weight: 1.132 kg

MS gy REDACTEDStep #13 Reconciliation - Blending

Calculate the yield.

- | | |
|---|-----------------|
| a. Theoretical Weight | <u>1.124</u> kg |
| b. Actual Weight Produced (Step # 12) | <u>1.132</u> kg |
| c. Waste (if any) | <u>0</u> kg |
| d. Total Accounted for (b+c) | <u>1.132</u> kg |
| e. Percent Yield $\{(d/a) \times 100\}$: | <u>101</u> % |

MS gy REDACTED

Master Record Approval

Prepared by: [Signature]Reviewed by: [Signature]Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision: 002Product Code: S818Batch Size: 1.12 U kgLot #: 702019Compression

By _____ Ck'd _____ Date _____

Step #14

Check the room and equipment for cleanliness, proper labeling and mechanical set-up. Complete room and equipment log books.

Room #: 111Equipment #: F-205MS 98Step # 15

Compress the blend from Step #12 into tablets on the tablet press equipped with the following specified tablet tooling according to the In-Process Tablet Specifications listed below:

Tablet Press Model: Heath Star Equipment #: F-205Tooling Size: 0.3430" x 0.6870"Shape: Oval shapeUpper Punch: PlainLower Punch: PlainIn-Process Tablet Specifications:a. Weight of 10 Tablets (g):

Upper Tolerance Limit	=	<u>8.095</u>	(+7%)
Upper Control Limit	=	<u>7.950</u>	(+6%)
Target Weight	=	<u>7.500</u>	g
Lower Control Limit	=	<u>7.050</u>	(-6%)
Lower Tolerance Limit	=	<u>6.975</u>	(-7%)

MS 98Master Record ApprovalPrepared by: [Signature]Reviewed by: [Signature]Approved by: [Signature]Date: REDACTEDDate: REDACTEDDate: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818 Batch Size: 1124 kg

Lot #: 202017

By Ck'd Date

Step #15 Con'tb. Hardness (5 tablets) (Tentative):

Upper limit = 10 kp
Target = 7 kp
Lower limit = 4 kp

c. Thickness: (Information only)d. Friability: Not more than 2% (10 tablets, 100 drops in a friabilator)

$$\frac{\text{Initial weight} - \text{Net weight}}{\text{Initial weight}} \times 100\% = \frac{7.462 - 7.432}{7.462} = 0.40\% \quad \text{MS} \quad \text{gy}$$

REDACTED

In-Process Compression Checks:

Remove ten (10) tablets every fifteen (15) minutes and perform Weight Variation, Thickness and Hardness tests. Perform Friability test at the beginning, middle and end of compression. Record results on In-Process Data Sheet.

Scale: Setra EL-200S Equipment #: S-055Hardness tester: VanKel VK200 Equipment #: F-194Friabilator: VanKel Equipment #: F-155

MS gy

REDACTED

Master Record Approval		
Prepared by: <u>[Signature]</u>	Reviewed by: <u>[Signature]</u>	Approved by: <u>[Signature]</u>
Date: <u>REDACTED</u>	Date: <u>REDACTED</u>	Date: <u>REDACTED</u>

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818 Batch Size: 1.124kg Date: 1.12.2017 Lot #: 202017 **REDACTED**

Product Code: 5010 Batch Size: 1000 Room Temperature: 20°C Room Humidity: 52%

Tablet press speed: 19.6 rpm Number of tooling installed: 4

X = reading

[illegible]

Master Record Approval

Prepared by:

Reviewed by:

Approved by: L. Saurage

Date:

Date: ~~REDACTED~~

Date: REJECTED

In-Process Data Sheet (1)

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

REDACTED

Product Code: S818 Batch Size: 1.124kg Date:

Lot #: 202201

Tablet press speed: 19.6 rpm

Number of tooling installed: 4

Room Temperature: 20°C

Room Humidity: 52%

X = reading

[illegible]

Master Record Approval

Prepared by:

Reviewed by: Spide

Approved by: K. M. M. M. M.

Date: ~~REDACTED~~

Date: REDACTED

Date: ~~REDACTED~~

In-Process Data Sheet (1)

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818 Batch Size: 1.124 kg Date: **REDACTED**
Lot #: **REDACTED**

Tablet press speed: 141.6 rpm
 Number of tooling installed: 4
 Room Temperature: 20 C
 Room Humidity: 52%

[illegible]

Master Record Approval

Prepared by: AMW dnt Reviewed by: syk Approved by: LMH
Date: REDACTED Date: REDACTED Date: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818 Batch Size: 1.124 kg Date: 1.12.2017 Lot #: 202017

Tablet press speed: 19.6 rpm Number of tooling installed: 4 Room Temperature: 20C Room Humidity: 52%

Weight of each Tablet from In-Process Data Sheet (1)

[illegible]

Master Record Approval

Prepared by: AM dyf Reviewed by: Syk Approved by: Seung
Date: REDACTED Date: REDACTED

Revision #: 002

REDACTED

Lot #: 202017

Room Temperature: 20°C**Weight of each Tablet from In-Process Data Sheet (1)**[illegible]

5/11/20

Reviewed by: Sph

Date: - UNACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818 Batch Size: 1.124 kg Date: REDACTED Lot #: REDACTED
 Tablet press speed: 19.6 rpm Number of tooling installed: 4 Room Temperature: 20°C Room Humidity: 52%

Tablet press speed: 19.6 rpm

Weight of each Tablet from In-Process Data Sheet (1)[illegible]

Master Record Approval

Prepared by: DAVID Reviewed by: such Approved by: LeSavage
Date: REDACTED Date: REDACTED Date: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1.124 kg

Lot #: 102017

By Ck'd Date

Step #16

Withdraw a 0.050 kg sample of tablets and submit for QC tests.

Gross: 0.073 kg Tare: 0.023 kg Net: 0.050 kg

MS sy

Step #17

Collect the remaining acceptable tablets in a clean, tared, properly identified drum lined with double polyethylene bags. Weigh and record the weights below.

Scale: Mettler PC 4400 Equipment #: S-004

Average weight of tablets: 748 mg
(from In-Process Record)

Gross Weight: 0.851 kg

Tare Weight: 0.038 kg

Net Weight: 0.813 kg

MS sy

Step #18

Reconciliation - Compression

Percent Yield:

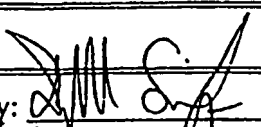


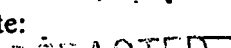
- a. Total Net Weight after compression (Step #17): 0.813 kg
(Excluding QC Samples)
- b. Total Net Weight of running rejects (tablets): 0.245 kg
- c. Samples removed for QC testing (Step #16): 0.050 kg
- d. Net Weight of remaining blend: 0 kg
- e. Other (Specify: Vacuum) 0.021 kg
- f. Total Net Weight Compression (a through e): 1.129 kg
- g. Total Net Weight after blending: 1.132 kg
(Step #12)
- h. Percent yield $\{ (f/g) \times 100\}$: 99.7 %

MS sy

Step #19

Move the drums to storage area and fill out inventory card.

MS sy

Master Record Approval		
Prepared by: 	Reviewed by: 	Approved by: 
Date: 	Date: REDACTED	Date: REDACTED

Andrx Pharmaceuticals, Inc.

aProduct: Metoprolol ER Tablets, 200 mg (Uncoated)

Page 1 of 15

Revision #: 002

Product Code #: S818 Batch Size: 1.125 kg Lot #: P02018

Description: White oval shaped tablets (0.3430" x 0.6870")

Issued by: [Signature] REDACTED

Date: _____

MASTER FORMULA

Item #	Ingredients	Weight %	Material Code #	Material Lot #/Rec. #	Amount per batch (kg)	Expiration Date	Weighted by	Checked by	Date
1.	Metoprolol Succinate ER Pellets	37.422	S817	28/-P02014	0.421			g	
2.	Metoprolol Succinate Active Pellets II	5.067	S816	P02013	0.057			g	
3.	Microcrystalline Cellulose, NF (Avicel PH-102)	7.822	2067	0103009	0.088			g	
4.	Microcrystalline Cellulose, NF (Avicel PH-200)	31.378	2168	9711028	0.353			g	
5.	Glycerol Monostearate 600P, NF	13.333	2055	0105105	0.150			g	
6.	Crospovidone (XL-10), NF	4.978	2008	9909043	0.056			g	
Total		100.0			1.125 kg				

COPY

Legal: [Signature]

REDACTED

METS18.002

Formula Approval		Batch Approval	
Prepared by: <u>[Signature]</u>	Date: _____	Reviewed by: <u>[Signature]</u>	Date: _____
Reviewed by: <u>[Signature]</u>	Date: _____	Approved by: <u>[Signature]</u>	Date: _____

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1125 kg

Lot#: P02018

Raw Material Weighing Record

PRECAUTION: WEAR SUITABLE RESPIRATOR AND DISPOSABLE GLOVES AT ALL TIMES
WHEN HANDLING THE PRODUCT OR RAW MATERIALS.

Step #1

By Ck'd Date

Check the room and all utensils including containers, polyethylene bags, covers, scoops, spatulas, etc. for cleanliness. Complete room log book.

Room #: 103

Step #2

Check all ingredients listed on page # 1 that will be used in the manufacturing process for name, material code#, receiving#, and expiration date.

Step #3

Weigh all ingredients and document on the "Material Weighing Record".

CP CP

CP CP

CP CP

REDACTED

Master Record Approval		
Prepared by: <u>[Signature]</u>	Reviewed by: <u>[Signature]</u>	Approved by: <u>[Signature]</u>
Date: REDACTED	Date: REDACTED	Date: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818 Batch Size: 1.125 kg Lot #: P02018

Material Weighing Record

Item #: 1

Name: Metoprolol Succinate ER Pellets

Code#: S817

Lot #: 2876 P02014

Scale #: 5-112

Gross: 0.429 kg

Tare: 0.008 kg

Net: 0.421 kg

Weighted by: CP

Date: REDACTED
Checked by: ac

Item #: 2

Name: Metoprolol Succinate Active Pellets II

RM Code#: S816

Receiving #: P0201

Scale #: 5-112

Gross: 0.063 kg

Tare: 0.006 kg

Net: 0.057 kg

Weighted by: CP

Date: REDACTED
Checked by: ac

Item #: 3

Name: Microcrystalline Cellulose, NF (Avicel PH-102)

RM Code#: 2067

Receiving #: 0103009

Scale #: 5-112

Gross: 0.094 kg

Tare: 0.006 kg

Net: 0.088 kg

Weighted by: CP

Date: REDACTED
Checked by: ac

Item #: 4

Name: Microcrystalline Cellulose, NF (Avicel PH-200)

RM Code#: 2168

Receiving #: 971023

Scale #: 5-112

Gross: 0.361 kg

Tare: 0.008 kg

Net: 0.353 kg

Weighted by: CP

Date: REDACTED
Checked by: ac

Item #: 5

Name: Glyceryl Monostearate 600P, NF

RM Code#: 2055

Receiving #: 0105105

Scale #: 5-112

Gross: 0.156 kg

Tare: 0.006 kg

Net: 0.150 kg

Weighted by: CP

Date: REDACTED
Checked by: ac

Item #: 6

Name: Crospovidone (XL-10), NF

RM Code#: 2008

Receiving #: 99090

Scale #: 5-112

Gross: 0.062 kg

Tare: 0.006 kg

Net: 0.056 kg

Weighted by: CP

Date: REDACTED
Checked by: ac

Item #:

Name:

RM Code#:

Receiving #:

Scale #:

Gross: kg

Tare: kg

Net: kg

Weighted by:

Date: REDACTED
Checked by:

Item #:

Name:

RM Code#:

Receiving #:

Scale #:

Gross: kg

Tare: kg

Net: kg

Weighted by:

Date: REDACTED
Checked by:

Master Record Approval

Prepared by:

Date:

Reviewed by:

Date:

Approved by:

Date:

REDACTED

REDACTED

REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818 Batch Size: 1.125 kg Lot #: PD2018

Blending

By Ck'd Date

Step #4

Check room and equipment for cleanliness, mechanical set-up and proper labeling.
Complete room and equipment log books.

Room #: 111 Equipment #: F-009 HA gy

Step #5

Check containers of all ingredients against formula page for name, material code #,
and amount. Check the weight of all the ingredients.

Scale #: S-004 HA gy

Step #6

Charge the following ingredients (Item # 3,4 and 6) into a suitable blender and
mix for 2 minutes.

Microcrystalline Cellulose, NF (Avicel PH-102) (Item #3)

Microcrystalline Cellulose, NF (Avicel PH-200) (Item #4)

Crospovidone (XL-10), NF (Item #6)

Model: TWINSHELL Equipment #: F-009 Size: 8 Quarts Speed: 23 R.P.M.

Time Start: 10:26 AM Time Stop: 10:28 AM Total Blending time: 2 Minutes HA gy

Step #7

Pass the mixture from Step # 6 through a hand screen (30 mesh size) or a Comil
equipped with a suitable size stainless screen (30 mesh equivalent) into clean, double
polyethylene bags.

Equipment #: 1A Screen Size: 30 HA gy

Master Record Approval

Prepared by: J. M. S. HA

Reviewed by: gyh

Approved by: J. M. S. HA

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol Succinate ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1.125 kg

Lot#: PD2018

By _____ Ck'd _____ Date _____

Step #8

Charge the screened mixture from Step #7 into a suitable blender and add Metoprolol Succinate ER Pellets (Item #1) and Metoprolol Succinate Active Pellets II (Item #2) into the blender.

Model: TWISTER

Equipment #: F-009

Size: 8 Quart

HA SY REDACTED

Step #9

Blend for fifteen (15) minutes.

Time Start: 10:35 AM Time Stop: 10:50 AM Speed: 23 R.P.M.

Total Blending Time: 15 minutes

HA SY REDACTED

Step #10

Pass the Glyceryl Monostearate, 600P (Item #5) by hand through a #30 mesh screen and add to the blend in Step #9.

SY HA REDACTED

Step #11

Blend for ten (10) minutes.

Time Start: 10:51 AM Time Stop: 11:01 AM Speed: 23 R.P.M.

Total Blending Time: 10 minutes

HA SY REDACTED

Master Record Approval

Prepared by: J.M. SA

Reviewed by: SPH

Approved by: L. Sarge

Date: REDACTED

Date: REDACTED

Date: REDACTED

REDACTED

REDACTED

REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818

Batch Size: 1.125 kg Lot #: PD2018

By _____ Ck'd _____ Date _____

Step #12

Collect the blend from Step #11 in a clean, tared, properly identified drum lined with double polyethylene bags. Weigh and record the weight of the blend.

Scale: S-004

Gross Weight: 1.167 kg

Tare Weight: 0.038 kg

Net Weight: 1.129 kg

HA Sy REDACTED

Step #13 Reconciliation - Blending

Calculate the yield.

a. Theoretical Weight	1.125 kg
b. Actual Weight Produced (Step # 12)	1.129 kg
c. Waste (if any)	0 kg
d. Total Accounted for (b+c)	1.129 kg
e. Percent Yield $\{(d/a) \times 100\}$:	100 %

HA Sy REDACTED

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision: 002

Product Code: S818

Batch Size: 1125 kg

Lot #:

P02018

Compression

By Ck'd Date

Step #14

Check the room and equipment for cleanliness, proper labeling and mechanical set-up. Complete room and equipment log books.

Room #: 111

Equipment#: F-205

AA 9

REDACTED

Step #15

Compress the blend from Step #12 into tablets on the tablet press equipped with the following specified tablet tooling according to the In-Process Tablet Specifications listed below:

Tablet Press Model: HEALTHSTAR Equipment #: F-205

Tooling Size: 0.3430" x 0.6870"

Shape: Oval shape

Upper Punch: Plain

Lower Punch: Plain

In-Process Tablet Specifications:

a. Weight of 10 Tablets (g):	
Upper Tolerance Limit	= 8.025 (+7%)
Upper Control Limit	= 7.950 (+6%)
Target Weight	= 7.500 g
Lower Control Limit	= 7.050 (-6%)
Lower Tolerance Limit	= 6.975 (-7%)

AA 9

REDACTED

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date:

Date: REDACTED

Date: REDACTED

REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818 Batch Size: 1.125 kg

Lot #: P02018

By _____ Ck'd _____ Date _____

Step #15 Con'tb. Hardness (5 tablets) (Tentative):

Upper limit = 10 kp
Target = 7 kp
Lower limit = 4 kp

c. Thickness: (Information only)d. Friability: Not more than 2% (10 tablets, 100 drops in a friabilator)

$$\frac{\text{Initial weight} - \text{Net weight}}{\text{Initial weight}} \times 100\% = \frac{7.482 - 7.451}{7.482} \times 100\% = 0.33\%$$

HD SY

REDACTED

In-Process Compression Checks:

Remove ten (10) tablets every fifteen (15) minutes and perform Weight Variation, Thickness and Hardness tests. Perform Friability test at the beginning, middle and end of compression. Record results on In-Process Data Sheet.

Scale: SERA

Equipment #: 5-191

Hardness tester: VANDEL

Equipment #: F-194

Friabilator: VANDEL

Equipment #: F-155

HD SY

REDACTED

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

In-Process Data Sheet (1)

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818 Batch Size: 1254 Date: 1/25/18

Tablet press speed: 19.5 rpm

Number of tooling installed: 4

Room Temperature:

50

Room Humidity:

50%

[illegible]

Master Record Approval

Prepared by:

Date:

Reviewed by:

Date:

Sigurd

by: SPK REFLECTED

Approved by: Dr. J. L. Hall

Date: REOACTED

In-Process Data Sheet (1)

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818
Batch Size: 1/25 kg
Date: 1/25/18
Lot #: P03018
REDACTED

Tablet press speed: 19.5 rpm
Number of tooling installed: 4
Room Temperature: 15°C
Room Humidity: 50%

[illegible]

Master Record Approval

Prepared by:

Reviewed by:

Approved by: L. Page

Date: ~~REDACTED~~

REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818 Batch Size: 1125 ¹²/₁₂ Date: 11/25/08 **REDACTED**

Lot #:

8/20/18

Product Code: S818 Batch Size: 125 kg Date: 1/25/24 Lot #: 1507
 Tablet press speed: 19.5 rpm Number of tooling installed: 4 Room Temperature: 15°C Room Humidity: 50%

Weight of each Tablet from In-Process Data Sheet (1)

[illegible]

Master Record Approval

Master Record Approval

Prepared by: [Signature] Approved by: [Signature]

Reviewed by: [Signature] Date: REDACTED

Date: REDACTED

Revision #: 002

In-Process Data Sheet (2)

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Product Code: S818 Batch Size: 1-125k Date: REDACTED Lot #: 022818

Product Code: S818 Batch Size: 1125 g Dose: 1000
 Tablet press speed: 19.5 rpm Number of tooling installed: 4
 Room Temperature: 15°C Room Humidity: 50%

Room Temperature: 15°C

Room Humidity: 50%

Weight of each Tablet from In-Process Data Sheet (1)

[illegible]

Master Record Approval

Master Record Approval

Prepared by: <u>[Signature]</u>	Reviewed by: <u>SNH</u>	Approved by: <u>[Signature]</u>
Date: <u>REDACTED</u>	Date: <u>REDACTED</u>	Date: <u>REDACTED</u>

Page 14 of 15

In-Process Data Sheet (2)

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

REDACTED

Product Code: S818 Batch Size: 1-125 kg Date: 7

Tablet press speed: 19.5 rpm Number of tooling installed: 4 Room Temperature: 15C Room Humidity: 50%

Weight of each Tablet from In-Process Data Sheet (1)

[illegible]

Master Record Approval

Prepared by: DAI/UA 27 Reviewed by: Sukh Approved by: 20000000
Date: REDACTED Date: REDACTED Date: REDACTED

Product: Metoprolol ER Tablets, 200 mg (Uncoated)

Revision #: 002

Product Code: S818 Batch Size: 1.125 kg Lot #: PO2018

By Ck'd Date

Step #16

Withdraw a 0.050 kg sample of tablets and submit for QC tests.

Gross: 0.073 kg Tare: 0.023 kg Net: 0.050 kg

HA SY REDACTED

Step #17

Collect the remaining acceptable tablets in a clean, tared, properly identified drum lined with double polyethylene bags. Weigh and record the weights below:

Scale: METLER PC 4400 Equipment #: S-004

Average weight of tablets: ^{EE 751 HA} 0.075 mg
(from In-Process Record)Gross Weight: 0.079 kg
Tare Weight: 0.038 kg
Net Weight: 0.041 kg

HA SY REDACTED

Step #18

Reconciliation - Compression

Percent Yield:

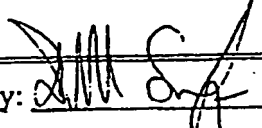


- a. Total Net Weight after compression (Step #17): 0.041 kg
(Excluding QC Samples)
- b. Total Net Weight of running rejects (tablets): 0.217 kg
- c. Samples removed for QC testing (Step #16): 0.050 kg
- d. Net Weight of remaining blend: 0 kg
- e. Other (Specify: Floor Reject): 0.015 kg
- f. Total Net Weight Compression (a through e): 1.123 kg
- g. Total Net Weight after blending:
(Step #12): 1.129 kg
- h. Percent yield $\{((f/g) \times 100\%)\}$: 99.5 %

HA SY REDACTED

Step #19

Move the drums to storage area and fill out inventory card.

HA SY REDACTED

Master Record Approval			
Prepared by: 	Reviewed by: 	Approved by: 	
Date: REDACTED	Date: REDACTED	Date: REDACTED	

MASTER FORMULA

Product: Metoprolol Succinate ER Pellets

Product Code #: S817 Batch Size: 7.772 kg Lot #: 022014

Description: White to Off-white Round Pellets

Issued by: Golden E. Nigam Date: REDACTED

Item #	Ingredients	Weight %	Material Code #	Material Lot #/Rec. #	Amount per batch (kg)	Expiration Date	Weighted by	Checked by	Date
1A.	Metoprolol Succinate Active Pellets II	70.549	S816	P02013	5.50				
1B.	Metoprolol Succinate Active Pellets II	N/A	S816	N/A	N/A		N/A	N/A	
2.	Eudragit S-100, NF (Methacrylic Acid Copolymer)	1.763	2102	0202008	0.137				REDACTED
3.	Cellulose Acetate Butyrate, PG (CAB 171-15)	24.550	2287	0106134	1.908				REDACTED
4.	Poloxamer 188, NF (Lutrol F-68)	2.981	2305	0109036	0.227				REDACTED
5.	Acetone, NF	**	2101	0202031	37.8				REDACTED
6.	Purified Water, USP	**	2014	0202104	4.2				REDACTED
		100.0	7.772						

NOTE: ** Evaporated during processing.

COPY

MetsS817.003

Master Record Approval

Batch Approval

Legal: REDACTED

Prepared by: REDACTED Date: REDACTED

Reviewed by: REDACTED Date: REDACTED

Approved by: REDACTED Date: REDACTED

Angel Carballido - ac

E. Cassola - P

Al Bello - CB

Ruben D. Rivera - PR

Day Bennett - DB

Eugene Joseph - aj

Eduardo Garcia - EG

LISHOMWA BARRETT - LB

RAFAEL SOLER - RS

Kyndel Morgan - KM

DEVON JOHNSON - DJ

MONGKOL SRIWONGTANYA - MS

Product: Metoprolol Succinate ER Pellets

Revision #: 003

Product Code: S817 Batch Size: 11.772 kg Lot #: P03014

Procedure

By _____ Ck'd _____ Date _____

Step #1

Check the weighing room and all utensils including containers, polyethylene bags, covers, scoops, spatulas, etc. for cleanliness. Check and complete the room logbook.

Room #: 103

ac @ REDACTED

Step #2

Check all ingredients listed on page # 1 that will be used in the manufacturing process for name, lot #/receiving #, material code # and expiration date shown on the drums.

ac @ REDACTED

Step #3

Dispense and weigh Acetone, NF (Item #5), Purified Water, USP (Item #6) in different suitable sizes of stainless steel containers.

Container for Acetone: 30 gallon
Container for Purified Water: 2 gallon

@ CB REDACTED

Step #4

Weigh all ingredients and document on the "Raw Material Weighing Record" (page #3) and the Master Formula page (page #1).

@ CB REDACTED

Master Record Approval		
Prepared by: <u>Sgh</u>	Reviewed by: <u>[Signature]</u>	Approved by: <u>[Signature]</u>
Date: <u>REDACTED</u>	Date: <u>REDACTED</u>	Date: <u>REDACTED</u>

Product: Metoprolol Succinate ER Pellets

Revision#: 003

Product Code: S817 Batch Size: 7.772 kg Lot #: P02014

Raw Material Weighing Record

Item #: 1A
Name: Metoprolol Succinate Active Pellets II
Code #: S816 Lot #: P02013
Scale #: 5-112
Gross: 6.352 kg
Tare: 0.852 kg
Net: 5.500 kg Date:
Weighed by: Checked by: U/D

Item #: 1B
Name: Metoprolol Succinate Active Pellets II
RM Code #: S816 Receiving #:
Scale #: N/A
Gross: kg
Tare: kg
Net: kg Date:
Weighed by: Checked by:

Item #: 2
Name: Eudragit S-100, NF (Methacrylic Acid Copolymer)
RM Code #: 2102 Receiving #: 9802001
Scale #: 5-112
Gross: 0.146 kg
Tare: 0.009 kg
Net: 0.137 kg Date:
Weighed by: Checked by: ac

Item #: 3
Name: Cellulose Acetate Butyrate, PG (CAB-171-15)
RM Code #: 2287 Receiving #: 0108134
Scale #: 5-112
Gross: 1.931 kg
Tare: 0.023 kg
Net: 1.908 kg Date:
Weighed by: Checked by: ac

Item #: 4
Name: Poloxamer 188, NF (Lutrol F-68)
RM Code #: 2305 Receiving #: 0109036
Scale #: 5-112
Gross: 0.236 kg
Tare: 0.009 kg
Net: 0.227 kg Date:
Weighed by: Checked by: ac

Item #: 5
Name: Acetone, NF
RM Code #: 2101 Receiving #: 0202031
Scale #: 5-182
Gross: 55.112 kg
Tare: 17.318 kg
Net: 37.794 kg Date:
Weighed by: Checked by: U/D

Item #: 6
Name: Purified Water, USP
RM Code #: 2014 Receiving #: 020221A4
Scale #: 5-112
Gross: 5.459 kg
Tare: 1.259 kg
Net: 4.200 kg Date:
Weighed by: Checked by: U/D

Item #:
Name:
RM Code #: N/A Receiving #:
Scale #:
Gross: kg
Tare:
Net: kg Date:
Weighed by: Checked by:

Master Record Approval

Prepared by: SMH Reviewed by:
Date: REDACTED Date: REDACTED Approved by: Savage
Date: REDACTED

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Acetone
 Code No.: 2101 Rec/Lot No.: 0202031
 Gross: 55.118 Exp. Date: REDACTED
 Tare: 17.318 Whg. By: (P)
 Net: 37.800 kg Ch'k By: (PB)
 Scale: 5-182 Date: REDACTED

To be used for:

Product: Metoprolol Succ. ER Pellets
 Code No.: 5817 Lot No.: P02014

FD#007

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Eudragit 5-100
 Code No.: 2102 Rec/Lot No.: 9802008
 Gross: 0.146 Exp. Date: REDACTED
 Tare: 0.009 Whg. By: (P)
 Net: 0.137 kg Ch'k By: (P)
 Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Pellets
 Code No.: 5817 Lot No.: P02014

FD#007

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Purified Water
 Code No.: 2014 Rec/Lot No.: 022021A4
 Gross: 5.459 Exp. Date: REDACTED
 Tare: 1.259 kg Whg. By: (P)
 Net: 4.200 kg Ch'k By: (PB)
 Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol Succ. ER Pellets
 Code No.: 5817 Lot No.: P02014

FPD#007

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: C.A. Butyrate
 Code No.: 2287 Rec/Lot No.: 0108134
 Gross: 1.931 kg Exp. Date: REDACTED
 Tare: 0.023 kg Whg. By: (P)
 Net: 1.908 kg Ch'k By: (P)
 Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Pellets
 Code No.: 5817 Lot No.: P02014

FPD#007

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: LuTrol F-68
 Code No.: 2305 Rec/Lot No.: 0109036
 Gross: 0.236 Exp. Date: REDACTED
 Tare: 0.009 kg Whg. By: (P)
 Net: 0.227 kg Ch'k By: (P)
 Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol ER Pellets
 Code No.: 5817 Lot No.: P02014

FPD#007

WEIGHING LABEL

Drum clean and tare ch'k by: N/A Date: N/A

Product: Metoprolol Succ. Act. Pellets II
 Code No.: 5816 Rec/Lot No.: P02013
 Gross: 6.352 kg Exp. Date: N/A
 Tare: 0.852 kg Whg. By: (P)
 Net: 5.50 kg Ch'k By: (PB)
 Scale: 5-112 Date: REDACTED

To be used for:

Product: Metoprolol Succ. Act. Pellets
 Code No.: 5817 Lot No.: P02014

FPD#007

Product: Metoprolol Succinate ER Pellets

Revision #: 003

Product Code: S817

Batch Size: 7.772 kg

Lot #: P03014

Procedure

By Ck'd Date

Step #5

Check the processing room and equipment for cleanliness, complete the room and equipment logbook.

Room #: 117

Equipment #: F-164

DB

Step #6

Check the materials for lot #/rec.#, code # and amount against the formula (page #1).
Check the weight of each ingredient.

Scale #: 5-183

Step #7

Mix Purified Water, USP (Item #6) and Acetone, NF (Item #5). Add Poloxamer 188 (Lutrol F-68), (Item #4), Cellulose Acetate Butyrate (CAB-171-15), PG (Item #3) and Eudragit S-100 (Methacrylic Acid Copolymer), NF (Item #2) into a mixture of Purified Water and Acetone while mixing with a mechanical stirrer until completely dissolved.

Equipment #: F-199

Start Time: 7:25 PM

Stop Time: 9:25 PM

Total Mix Time: 1 hr

Step #8

Proceed to the In-Process Data Sheet for equipment set-up.

Tentative coating conditions are:

Product temperature: 20- 40°C

Atomization pressure: 1 - 3 bars

Pump rate: 3 - 200 mL/min

Master Record Approval

Prepared by: [Signature]

Reviewed by: [Signature]

Approved by: [Signature]

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol Succinate ER Pellets

Revision#: 003

Product Code: S817

Batch Size:

7.772 kg

Lot #:

P02014

Procedure

By Ck'd Date

Step #9

Load the Metoprolol Succinate Active Pellets II (Item #1A and 1B) to the fluidized bed coater and spray the coating suspension from Step #7 onto the pellets. Record the coating conditions on the In-Process Data Sheet (pages 8 to 13).

Remove 1.0 kg of coated pellets when 31.65 kg of coating solution has been consumed. Label "26 % coating level P02014" on product container.

Remove 1.0 kg of coated pellets when 41.14 kg of coating solution has been consumed. Label "28 % coating level P02014" on product container.

Remove the rest of coated pellets when coating solution has been completely consumed. Label "30 % coating level P02014" on product container of final product.

Note: Spray slowly at the beginning to avoid agglomeration.

EG. ~~P02~~ REDACTED

Step #10

After the coating solution from Step #7 has been consumed, stop the pump and dry the final pellets in the fluidized bed coater for 2 minutes. Remove pellets from the Glatt machine and continue drying in an oven.

Suggested Guidelines for Drying in an Oven

Equipment #: F-207

Temperature: Setting $40 \pm 10^{\circ}\text{C}$ Drying Time Start: 12:00 AM Drying Time Stop: 12:00 AM Total Drying Time: 24 hrsLOD Equipment #: F-190 (Note: set the temperature to 105°C)For 26 % coating levelSample Weight: 3.237 g% Loss on Drying (LOD): 0.479 %For 30 % coating levelSample Weight: 4.09 g% Loss on Drying (LOD): 0.293 %For 28 % coating levelSample Weight: 4.168 g% Loss on Drying (LOD): 0.319 %

P02 MS REDACTED

Master Record Approval

Prepared by: SylReviewed by: [Signature]Approved by: L. Savage

Date:

Date:

Date:

REDACTED

REDACTED

REDACTED

Product: Metoprolol Succinate ER Pellets

Revision#: 003

Product Code: S817

Batch Size: 7.772 kg

Lot #: PD2014

Procedure

By Ck'd Date

Step #11

When the drying is completed, collect the pellets in clean, tared, properly identified drums or containers lined with double polyethylene bags. Record the weight.

Scale #: S-112

For 26 % coating level

Gross: 1.011 kg Tare: 0.037 kg Net: 0.974 kg

MS MC

For 28 % coating level

Gross: 1.027 kg Tare: 0.037 kg Net: 0.99 kg

MS MC

For 30 % coating level

Gross: 5.528 kg Tare: 0.046 kg Net: 5.482 kg

MS MC

REDACTED

Step #12

Screen the pellets from Step #11 on 30 mesh and 60 mesh. Collect the pellets between 30 and 60 mesh. Remove approximately 0.02 kg sample for QC testing.

Scale #: S-028

For 26 % coating level

Gross: 0.0336 kg Tare: 0.0136 kg Net: 0.020 kg

Sg MS

For 28 % coating level

Gross: 0.0334 kg Tare: 0.0134 kg Net: 0.020 kg

Sg MS

For 30 % coating level

Gross: 0.0336 kg Tare: 0.0136 kg Net: 0.020 kg

Sg MS

REDACTED

Master Record Approval

Prepared by: Sg

Reviewed by: [Signature]

Approved by: L. Savage

Date: REDACTED

Date: REDACTED

Date: REDACTED

Product: Metoprolol Succinate ER Pellets

Revision#: 003

Product Code: S817

Batch Size: 7.772 kg

Lot #: P82014

Procedure

By Ck'd Date

Step #13

Record the weight of acceptable Pellets from Step #12.

Scale #: 5-02 208

For 26 % coating level

Gross: 0.979 kg Tare: 0.037 kg Net: 0.942 kg

Sy mro

For 28 % coating level

Gross: 0.999 kg Tare: 0.037 kg Net: 0.962 kg

Sy mro

REDACTED

For 30 % coating level

Gross: 5.471 kg Tare: 0.046 kg Net: 5.425 kg

Sy mro

Step #14 - Batch Accountability

- (a) Sample weight for % LOD Analysis (Step #10) 0.011 kg
- (b) Sample weight for QC testing (Step #12) 0.060 kg
- (c) Weight of acceptable pellets (Step #13) 7.329 kg
- (d) Weight of all in-process rejects: 0.291 kg
- (e) Actual yield (a+b+c+d): 7.691 kg
- (f) Theoretical Yield: 7.772 kg
- (g) Percent accountable for (e/f x 100): 99 %

MS Sy

Step #15

Move drums to storage area.

MS Sy

REDACTED

Master Record Approval			
Prepared by: <u>Sy</u>	Reviewed by: <u>Sy</u>	Approved by: <u>L. Savage</u>	
Date: <u>REDACTED</u>	Date: <u>REDACTED</u>	Date: <u>REDACTED</u>	

In-Process Data Sheet

Revision #: 003

P03014

Lot #: _____

Batch Size: 7772

Product Code: S817

Product: Metoprolol Succinate ER Pellets

Equipment Set-Up: _____

Machine Model #: 6800-15

Pump Model #: Masterflex

Column Height: 30mm

Tube Size: 16mm

Equipment #: F-164

Equipment #: F-126

Nozzle Size: 1.2mm

Insert Type: Waster

Plate Type: A

Shaking Interval: 30min

Size: 9"

Inlet Air Regulation Flap: 100%

Shaking time: 3sec

Comments: _____

Date: REDACTED

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
9:10pm	10.0	0.00	147.44	29.79	2.8	33.25	33.76	37.65	156.52	17.66	EG	start spray
9:25pm	13.0	0.10	143.78	33.94	2.8	31.83	32.54	36.72	153.53	16.40	DB	
9:40pm	16.0	0.26	147.50	38.33	2.8	31.03	31.79	36.38	153.10	17.49	EG	
9:55pm	14.0	0.46	142.01	35.53	2.8	30.20	30.86	36.06	153.21	14.52	EG	
10:10pm	20.0	0.69	148.86	40.78	2.8	24.27	24.93	35.57	157.01	16.09	DB	
10:25pm	25.0	0.96	144.76	42.24	2.8	28.81	29.47	35.57	154.81	15.06	DB	
10:40pm	28.0	1.28	145.54	47.25	2.8	28.08	28.86	35.42	146.27	17.08	DB	
10:55pm	31.0	1.62	146.13	43.95	2.8	27.78	28.37	35.40	148.71	13.87	DB	
11:10pm	34.0	2.00	148.47	51.76	2.8	27.34	27.91	35.38	154.57	13.94	EG	
11:25pm	37.0	2.32	144.37	43.46	2.8	26.68	27.17	35.28	156.52	15.37	EG	

Master Record Approval

Approved by: L. Hargre

Date: REDACTED

Reviewed by: [Signature]

Date: REDACTED

Prepared by: Sph

Date: REDACTED

Andrx Pharmaceuticals, Inc.

In-Process Data Sheet

Product: Metoprolol Succinate ER Pellets Product Code: S817 Batch Size: 7.772 kg Lot #: P13014

REDACTED

Date: _____

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
11:40am	40.0	2.82	151.33	51.64	2.8	27.17	27.61	35.42	152.37	15.64	EG	
12:10pm	40.0	3.78	149.81	60.68	2.8	25.65	26.51	35.30	151.66	15.03	DB	
12:40pm	40.0	4.76	147.50	70.08	2.8	25.66	26.39	35.35	146.51	17.8	DB	
1:10pm	40.0	5.74	145.93	69.83	2.8	25.61	26.49	35.79	150.42	15.75	EG	
1:40pm	40.0	6.66	152.38	74.96	2.8	25.68	26.54	35.13	145.05	17.22	EG	
2:10pm	40.0	7.64	150.13	87.78	2.8	25.07	25.68	34.62	152.13	16.53	EG	
2:40pm	40.0	8.62	148.47	92.14	2.8	24.78	25.46	34.40	161.80	16.16	EG	
3:10pm	40.0	9.58	151.79	100.11	2.8	24.78	25.63	34.35	155.30	16.98	EG	
3:40pm	40.0	10.56	152.47	109.39	2.8	24.54	25.34	34.69	160.66	17.18	EG	
4:10pm	40.0	11.52	153.75	109.02	2.8	24.98	26.05	35.03	157.99	17.29	DB	
4:40pm	40.0	12.48	157.46	116.35	2.8	24.85	25.73	34.94	153.84	16.64	DB	
5:10pm	40.0	13.46	151.79	126.60	2.8	24.65	25.51	34.81	147.24	15.54	EG	
5:40pm	40.0	14.42	156.68	124.65	2.8	24.93	25.48	35.01	144.95	17.29	EG	
6:10pm	40.0	15.38	160.58	133.71	2.8	24.93	25.73	35.11	154.0	16.14	EG	

REDACTED

Master Record Approval

Approved by: [Signature]

Reviewed by: [Signature]

Date: REDACTED

Date: REDACTED

Prepared by: Sph

Date: REDACTED

Andrx Pharmaceuticals, Inc.

Revision #: 003

In-Process Data Sheet

Product: Metoprolol Succinate ER Pellets Product Code: S817 Batch Size: 7.772 kg Lot #: PO2014

Date: REDACTED

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
6:40	40.0	16.51	168.13	149.79	2.3	24.55	26.10	35.11	151.64	17.46	US	
7:10	40.0	17.30	165.47	141.38	2.8	25.10	26.54	35.58	151.40	17.66	US	
7:40	40.0	18.26	163.71	145.46	2.8	25.10	26.61	34.81	150.98	16.43	US	
8:10	40.0	19.32	161.91	152.10	2.8	25.27	26.20	35.15	168.49	17.87	US	
8:40	40.0	20.28	162.71	162.25	2.7	25.12	26.64	35.11	159.56	14.65	US	
9:10	40.0	21.24	166.84	175.31	2.8	25.27	26.17	35.18	160.67	16.16	US	
9:40	40.0	22.18	168.73	181.17	2.8	25.56	26.78	35.23	171.42	17.50	US	
10:10	40.0	23.11	172.20	175.57	2.7	25.16	26.37	35.28	152.77	17.18	US	
10:40	40.0	24.07	172.76	179.35	2.7	25.63	26.78	35.42	157.71	17.11	US	
11:10	40.0	25.04	176.35	185.60	2.7	25.73	26.44	35.28	159.94	17.05	US	
11:40	40.0	26.00	174.24	201.81	2.7	25.71	26.39	35.47	169.71	17.05	US	
12:10	40.0	26.94	181.06	221.50	2.8	25.63	26.54	35.21	164.39	16.81	US	
12:40	40.0	27.90	172.50	214.58	2.8	25.76	26.61	35.40	163.36	16.34	US	
13:10	40.0	28.86	180.32	222.51	2.8	25.90	26.88	35.57	168.95	16.19	US	

REDACTED

Master Record Approval

Prepared by: Sybil Reviewed by: [Signature] Approved by: [Signature]
 Date: REDACTED Date: REDACTED Date: REDACTED

Andrx Pharmaceuticals, Inc.

In-Process Data Sheet

Revision #: 003

PD3014

Product: Metoprolol Succinate ER Pellets

Product Code: S817 Batch Size: 7.773 kg Lot #:

Date: REDACTED

Time	Pump Rate Reading (mL/min)	Weight Consumed (kg)	PD Product (mmHg)	PD Outlet Air Filter (mmHg)	Actual Atomization Pressure (bar)	Outlet Air Temperature (°C)	Product Temperature (°C)	Inlet Air Temperature (°C)	Air Volume (SCFM)	Inlet Dew Point (°C)	Done by	Comments
1:40	40.0	29.98	178.34	234.77	2.8	25.81	26.76	35.84	155.35	17.47	PRC	
3:10	40.0	30.74	172.70	228.32	2.8	25.95	27.00	36.21	162.52	18.69	PRC	
2:40	40.0	31.65	176.36	235.99	2.8	26.05	26.78	36.11	166.05	17.90	PRC	
3:10	40.0	32.62	175.04	250.10	2.7	26.14	17.44	36.24	156.13	17.08	PRC	
3:40	40.0	32.62	175.17	253.08	2.5	26.39	27.61	37.26	156.79	19.23	PRC	
4:10	40.0	32.57	180.32	253.01	2.8	27.00	29.81	39.45	157.26	17.32	PRC	
4:40	40.0	35.14	180.72	257.97	2.8	27.88	29.96	40.75	157.01	16.98	MS	
5:10	40.0	36.40	180.32	262.97	2.8	29.20	29.96	39.36	167.76	17.52	PRC	
5:40	40.0	37.36	175.26	269.68	2.8	27.73	29.03	38.28	166.65	17.46	PRC	
6:10	40.0	37.66	182.13	280.31	2.8	27.54	29.35	37.91	168.00	17.49	PRC	STOP Per Sample
6:40	40.0	37.66	153.02	73.01	2.8	27.66	30.49	36.06	153.72	20.27	PRC	DIMTED SPEAKING
6:50	40.0	38.62	160.18	206.04	2.8	27.20	29.22	37.28	162.80	19.92	PRC	
7:10	40.0	38.52	157.22	226.10	2.8	27.03	29.28	37.28	153.10	19.73	PRC	
7:40	40.0	40.50	146.17	172.55	2.8	27.15	29.51	38.40	154.71	17.54	PRC	

Master Record Approval

Approved by: LSH

Date: REDACTED

Reviewed by: MSH

Date: REDACTED

Prepared by: MSH

Date: REDACTED

In-Process Data Sheet

Revision #: 003

Product: Metoprolol Succinate ER Pellets Product Code: S817 Batch Size: 7.77 g Lot #: 2

Date:

[illegible]

~~ALL INFORMATION CONTAINED HEREIN IS UNCLASSIFIED~~

Master Rec'd Approval

Prepared by: Spoke Approved by: L. Savage
Date: REDACTED Date: REDACTED

In-Process Data Sheet

PD2014

Product Code: S817 Batch Size: 7776 kg Lot #: 7776

Product: Metoprolol Succinate ER Pellets

Date:

[illegible]

~~REDACTED~~

Master Record Approved

Approved by: LS

Approved: _____
Date: _____

Reviewed by:

~~DATE DACTED~~

Approved by: _____
Sgt. _____

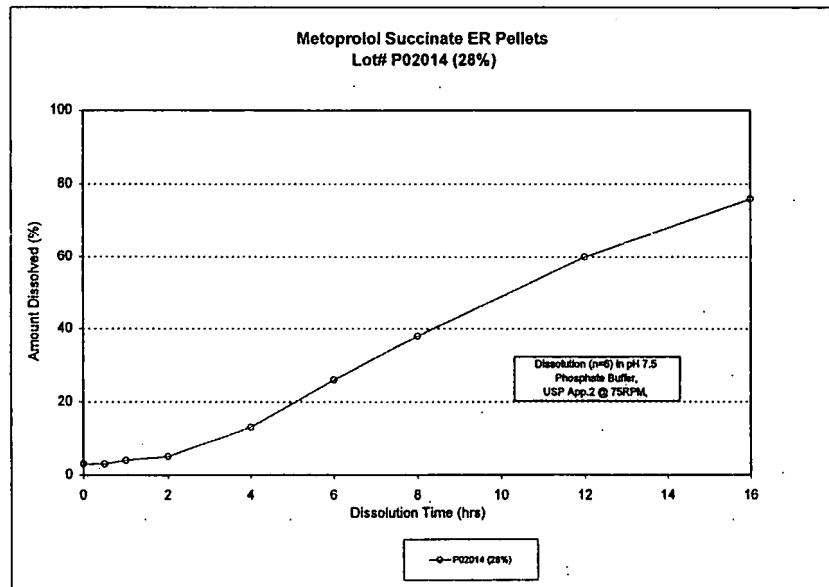
Date: _____

REDACTED

Metoprolol Succinate ER Pellets
Lot# P02014 (28%)
Dissolution (n=6) in pH 7.5 Potassium Phosphate Buffer

P02014 (28%)
 USP App. 2
 75 rpm
 pH 7.5 Buffer
 Hanson
 UV Analysis: 280nm
 Cellpath: 10.0mm

Amount Dissolved (%)										
Time (hr)	V1	V2	V3	V4	V5	V6	Mean	%RSD	Min	Max
0	3	2	2	3	5	2	3	42	2	5
0.5	4	3	3	4	6	2	3	38	2	6
1	4	3	3	4	6	2	4	37	2	6
2	5	4	4	5	7	3	5	28	3	7
4	13	12	12	14	16	12	13	11	12	16
6	25	23	24	26	30	25	26	9	23	30
8	37	35	37	39	46	37	38	10	35	46
12	59	56	58	60	69	59	60	8	56	69
16	74	72	73	75	85	74	76	7	72	85

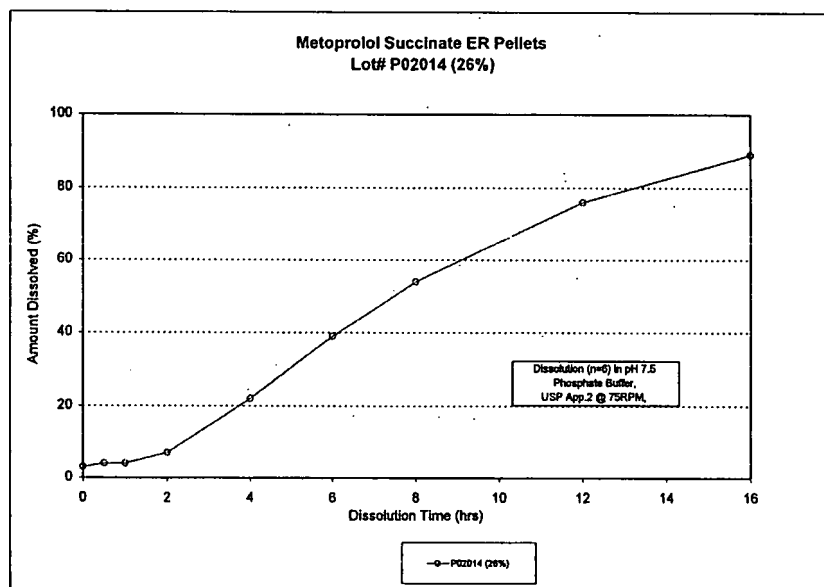


REDACTED

Metoprolol Succinate ER Pellets
Lot# P02014 (26%)
Dissolution (n=6) in pH 7.5 Potassium Phosphate Buffer

P02014 (26%)
 USP App. 2
 75 rpm
 pH 7.5 Buffer
 Hanson
 UV Analysis: 280nm
 Cellpath: 10.0mm

Amount Dissolved (%)										
Time (hr)	V1	V2	V3	V4	V5	V6	Mean	%RSD	Min	Max
0	4	3	3	4	4	2	3	26	2	4
0.5	5	3	4	5	5	3	4	22	3	5
1	5	4	4	5	5	3	4	22	3	5
2	7	6	6	7	8	5	7	15	5	8
4	23	22	22	22	25	21	22	6	21	25
6	40	39	38	39	42	38	39	4	38	42
8	55	54	54	54	57	53	54	3	53	57
12	77	76	76	76	78	75	76	2	75	78
16	90	88	88	89	91	88	89	1	88	91



LABORATORY NOTEBOOK

Notebook No.: SR 1860

Assigned to: Mongkol Siwongjanya

Date: REDACTED

Use Nalge Cat. No.

6301-1000

to reorder.

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REDACTED

		gm/batch
1	cellulose 20B	240
2	Metoprolol succinate	600
3	Methocel E5	30
4	Tween 80	0.5
5	Water	1800
total		870

REDACTED

FOR UNIGLATT

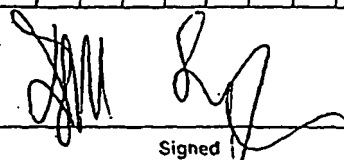
Date: _____ Lot number: SA1860-71 Equipment number: F-125
Set up (drive one): _____ Top spray: microtized Bottom spray (cone): _____
Filter bag: _____ screen: 1.0
Nucleus size (mm): 0.8 B: C
plate: _____
Cylinder height: _____
specimen: _____
Yes: _____ No: _____ Autoheater: ON OFF

Time	SPR rate ml/min	PD product	PD rate g/hr	Heat exchanger press. (psi)	Dist. Temp. (°C)	Inlet Temp. (°C)	Dist. at flow (°C)	Dist. by	Remarks
9:30	2.0	0.5	0.2	1.5	40	62	35%	g	column - 15 min
10:00	2.5	0.5	0.2	1.5	42	62	35%	g	
10:30	3.0	0.4	0.2	1.5	44	62	35%	g	
11:00	3.5	0.4	0.2	1.5	46	64	35%	g	
11:30	4.0	0.4	0.5	1.5	44	64	35%	g	
12:00	4.5	0.4	0.6	1.5	43	62	35%	g	
12:30	5.0	0.5	0.8	1.5	42	64	35%	g	Increase water solution flow
1:00	5.5	0.5	0.9	1.5	42	66	35%	g	
1:30	6.0	0.5	1.1	1.5	42	70	35%	g	
2:00	6.0	0.5	1.3	1.5	43	70	35%	g	
2:30	6.0	0.5	1.3	1.5	43	70	35%	g	
3:00	6.0	0.5	1.4	1.5	43	70	35%	g	
3:30	6.0	0.5	1.6	1.5	43	74	35%	g	
4:00	6.0	0.5	1.6	1.5	43	74	35%	g	
4:30	6.0	0.5	1.6	1.5	44	74	35%	g	
5:00	6.0	0.6	1.9	1.5	44	74	35%	g	
5:36	end								N = 849.9
5:41	stop	dry							

REDACTED

Continued on Page _____

Read and Understood By



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REDACTED

Date

Signed

REDACTED

Date

REDACTED

	gms/batch
1 SR 1860-31	435
2 Metoprolol succinate	300
3 Methocel ES	15
4 Tween 80	0.25
5 Water	900
Total	750.25

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR1860-32 Equipment number: E-003

Set up (circle one):

Filter bag:

Nozzle size (mm):

plate:

column height:

spacer:

Top spray

micronized

0.8

A

Yes

Bottom spray (Wurster)

screen

1.0

B

No

1.2

C

Autoshaker: ON OFF

Bottom spray (cone)

Time	spray rate ml/min	PO product	PO outlet air filter	Actual start/stop press. (bar)	Outlet Temp. (C)	Inlet Temp. (C)	Outlet air flow	Done by	Comments
10:17	4.0	0.3	0.6	1.5	40	63	30%	MLP	
10:41	6.0	0.3	0.8	1.5	43	65	30%	MLP	
11:17	6.0	0.3	1.5	1.5	44	61	30%	MLP	
11:47	6.0	0.3	1.8	1.5	45	66	30%	MLP	
12:22	6.0	0.3	2.8	1.5	45	65	30%	MLP	
12:52	7.0	0.3	2.4	1.5	46	70	30%	MLP	
1:22	7.0	0.3	2.6	1.5	44	61	30%	MLP	
1:52	7.0	0.3	2.4	1.5	45	61	30%	MLP	
2:22	7.0	0.3	2.6	1.5	44	60	30%	MLP	
2:52	7.0	0.3	2.8	1.5	45	61	30%	MLP	
3:22	7.0	0.3	3.0	1.5	45	62	30%	MLP	
3:28	0	0.3	3.1	1.5	45	62	30%	MLP	Finish specking
3:33	Finish	orig							n=732.98

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Continued on Page _____

Signed _____

REDACTED

Date _____

Read and Understood By

Signed _____

Date _____

REDACTED

Date _____

REDACTED

	g/m/batch
1 SR 1860-31	435
2 Metoprolol succinate	300
3 Methocel E5	15
4 Triacetin 80	0.25
5 Water	900
Total	750.25

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR 1860-33 Equipment number: E-125

Set up (circle one): Top spray micronized Bottom spray (Wurster) Bottom spray (cone)

Filter bag: _____

Nozzle size (mm): 0.8 1.2

Plate: A B C D

Column height: 20 mm

Spacer: Yes No

Autoshaker: ON OFF

Time	Spray rate ml/min	PO product	PO outlet at filter	Actual atomization press. (bar)	Outlet Temp. (°C)	Inlet Temp. (°C)	Outlet at top	Down by	Comments
10:15	4.0	0.5	0.2	1.5	40	62	35%	M.R.D.	
10:45	5.0	0.6	0.4	1.5	44	62	35%	M.R.D.	
11:15	6.0	0.7	1.4	1.5	45	61	35%	M.R.D.	
11:45	6.0	0.6	2.4	1.5	44	63	35%	M.R.D.	
12:20	6.0	6.6	2.6	1.5	43	64	35%	M.R.D.	
12:50	6.0	0.6	2.7	1.5	44	63	35%	M.R.D.	
1:20	7.0	0.6	3.1	1.5	45	64	35%	M.R.D.	
1:50	7.0	0.7	3.4	1.5	44	63	35%	M.R.D.	
2:20	7.0	0.7	3.1	1.5	45	63	35%	M.R.D.	
2:50	7.0	0.7	3.3	1.5	45	63	35%	M.R.D.	
2:55	0	0.7	3.4	1.5	45	62	35%	M.R.D.	Finish spraying
3:20	Finish drying								N=675.4g

REDACTED

Continued on Page _____

Read and Understood By

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REDACTED

Date

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REDACTED

Date

REDACTED

SR1860-36	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	70	SR1860-32	70 to 30
CAB 171-15 P6	28.57	20	0011048	67 to 33
ATEC	0.00	0	000004724	
PEG 400	14.29	10	0500253	67 to 33
Total batch	142.86	100		
Total coating	42.86			
Acetone	700.00			
Coating solution conc	5.77			
Total weight of coating	742.86			
Take 10 gm at 20 % coating	194.13	10		
Take 10 gm at 20 % coating	433.33	20		

REDACTED

FOR UNIGLATT

Date: _____ Lot number: 28R6-85 Equipment number: E-044

Set up (check one):
Fill bag: _____
Hazard site a leak:
plate: _____
calorie light:
source: _____

Top spray
instructed:
S.I.
A
2000 ft
Yes

Bottom spray (Hazard):
screen
S.I.
B
No

Bottom spray (cont):
C
D
Aviso-hazak: ON OFF

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Read and Understood By

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Date

REDACTED

SR1860-37	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	70	SR1860-32	70 to 30
CAB 171-15-16	28.57	20	0011048	67 to 16.5 to 16.5
ATEC	7.14	5	0000011724	67 to 16.5 to 16.5
PEG 400	7.14	5	050253	67 to 16.5 to 16.5
Total batch	142.86	100		
Total coating	42.86			
Acetone	700.00			
Coating solution conc	5.77			
Total weight of coating	742.86			
Take 10 gm at 20 % coating	184.13	10		
Take 10 gm at 20 % coating	433.33	20		

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR 1860-37 Equipment number: E-125

Set up (check one): Top spray: micronized Bottom spray (Mikrolar): screen Bottom spray (conal): screen

Filter bag: _____ Nozzle size (mm): 0.8 1.3 1.5 2.0 2.5 3.0 3.5 4.0 5.0 6.0 8.0 10.0 12.5 15.0 17.5 20.0 22.5 25.0 27.5 30.0 32.5 35.0 37.5 40.0 45.0 50.0 55.0 60.0 65.0 70.0 75.0 80.0 85.0 90.0 95.0 100.0

plate: A B C D

column height: 20.0 25.0 30.0 35.0 40.0 45.0 50.0 55.0 60.0 65.0 70.0 75.0 80.0 85.0 90.0 95.0 100.0


operator: Yes No Auto/bake: ON OFF

Time	Top spray	Bottom spray	Filter bag	Nozzle size	Column height	Plate	Column height	Operator
11:00	3.0	0.3	0.1	1.5	30	2.3	30%	mic
11:35	3.0	0.3	0.1	1.5	30	2.0	20%	mic
11:50	3.5	0.3	0.1	1.5	21	2.0	20%	mic
12:05	4.0	0.3	0.4	1.5	28	2.0	30%	mic
12:20	4.5	0.3	1.2	1.5	28	2.0	30%	mic
12:35	5.0	0.4	1.4	1.5	28	2.0	30%	mic
12:50	5.0	0.8	1.6	1.5	28	2.0	30%	mic Takes sample at 12:50
1:05	5.0	0.9	1.9	1.5	28	2.0	30%	mic
1:20	5.0	0.9	1.9	1.5	28	2.0	30%	mic
1:35	5.0	0.9	1.9	1.5	28	2.0	30%	mic
1:50	5.0	0.9	2.1	1.5	28	2.0	30%	mic
2:05	5.0	0.9	2.2	1.5	28	2.0	30%	mic Takes sample at 2:05 One bulk up on nozzle tip.
2:20	5.0	0.9	2.2	1.5	28	2.0	30%	mic
2:35	5.0	0.9	2.5	1.5	28	2.0	30%	mic
2:50	5.0	0.9	2.8	1.5	28	2.0	30%	mic
3:05	5.0	0.9	2.8	1.5	28	2.0	30%	mic
3:20	6.0	0.9	3.0	1.5	28	2.0	30%	mic
3:40	0	0.4	3.5	1.5	28	2.0	30%	mic Finish spraying
3:43	Finish	2.4						mic n=107.19t
								Reject n=5.78

REDACTED

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Date



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Date

REDACTED

	SR1060-38	2776batch	%	Lot #	Ratio
✓ Metapropyl Succinate pellets	100.00	90		SR1060-32	90 to 40
✓ CAB	26.19	25			2 to 1.5
✓ ATEC	6.05	5			
✓ PEG 400	22.67	17			2 to 1.5
Total batch	156.97	100			
Total coating	56.67				
✓ Macerals	1200.00				
Coating solution conc	8.30				
Total weight of coating	1206.67				
Take 10 gm at 20 % coating	476.50	20			
Take 10 gm at 30 % coating	614.29	30			
Final=20 % coating	1206.73				

thru #25

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR 186-35 Equipment number: 1-004

Set up (circle one):	Top spray	Bottom spray (fluror):	Solane spray (cool)
Filter bag:	micronized	green	
Nozzle size (mm):	0.8	1.0	1.2
plate:	A	B	C
column height:	20 cm		
spacer:	Yes	No	Autohaker: ON
			OFF

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Date _____

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REDACTED

SR1660-3	g/batch	%	Lot #	Ratio
Metacrylic Succinate pellets	100.00	50	SR1660-32	60 to 40
CAB	53.33	30		2 to 1 to 1
Rural EF	18.87	10		2 to 1 to 1
PEG 400	18.87	10		2 to 1 to 1
Total batch	190.07	100		
Total coating	58.67			
Acetone	100.00			
water	200.00			
Coating solution conc.	1.35			
Total weight of coating	1286.87			
Take 10 gm at 20 % coating	50.00	30		
Take 10 gm at 30 % coating	84.36	30		
Final=40 % coating	1284.73	40		

Cleanse Rural EF in water first and slowly add the solution to polymer solution

→ Dissolve 100ul EF in water first and slowly add the solution to polymer solution

- * See Mac before adding Kneel solution

REDACTED

FOR UNGLATT

Date: _____ Lot number: SLIP66-89 Equipment number: E-125

Set up (circle one): Filter bag: Nozzle size (mm): plate: column height: spacer:	Top spray intermixed: 0.8 A 20-25 Yes	Bottom spray (Wanted): green 1.2 C Autobaker: ON	Bottom spray (cone) D OFF
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Date _____

REDACTED

SR1860-40	gm/batch	%	Lot #	Ratio
Meloprolol Succinate pellets	100.00	60	SR1860-32	60 to 40
CAB	50.00	30		2.25 to 0.75
ATEC	0.00	0		
PEG 400	16.67	10		2.25 to 0.75
Total batch	166.67	100		
Total coating	66.67			
Acetone	1000.00			
water	200.00			
Coating solution conc	5.26			
Total weight of coating	1266.67			
Take 10 gm at 20 % coating	550.00	20		→ 22.2%
Take 10 gm at 30 % coating	942.86	30		→ 33.7%
Final=40 % coating	1266.73	40		

REDACTED

FOR UNIGLATT.

Date: _____ Lot number: SR160-90 Equipment number: F-135

Set up (check one):
Filter bag: _____
Nozzle size (mm): 0.8
plate: A
column height: _____
easier: _____

Top spray autoclaved: _____
Bottom spray (Wash): scout
1.0 1.2
B C
D

Autoshac: ON OFF

Time	Top up rate ml/min	PO product	PO index at 100	Actual concentration ppm (cal)	Output Temp °C	Inlet Temp °C	Output at 100	Down by	Comments
9:45 AM	3.0	0.7	0.1	1.5	24	18	35%	5g	
10:00 AM	0.5	0.8	0.3	1.5	26	26	36%	N3	
10:25 AM	0.0	0.7	0.5	1.5	28	25	35%	N3	
11:30 AM	0.5	0.7	0.7	1.5	28	26	35%	N3	
12:05 PM	3.0	0.7	1.3	1.5	28	26	36%	N3	
1:00 PM	5.5	0.9	1.9	1.5	28	26	35%	N3	
11:30 AM	5.5	0.9	2.0	1.5	28	26	35%	5g	
12:00 PM	5.5	0.7	2.1	1.5	27	24	35%	N1	
2:15 PM	5.5	0.7	2.4	1.5	28	26	35%	N3	Water sample 1:78 g/L (200 ml) at 1:30 pm 195 g/L
2:30 PM	6.5	0.7	2.6	1.5	28	22	35%	N3	
1:00 PM	5.5	0.7	3.0	1.5	28	22	35%	5g	
2:30 PM	5.5	0.6	2.8	1.5	27	26	35%	N3	Water sample 0.77 g/L (30 L) at 1:30 pm 192 g/L
2:30 PM	5.5	0.5	3.4	1.5	28	28	35%	N0	
2:40 PM	0	0.5	4.1	1.5	28	27	35%	N3	Finish washing → dry for 3m at 1:50 PM Water sample = 173 g/L at 1:50 PM 174 g/L

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Date _____

REDACTED

SR1860-41	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	60.00	SR1860-32	60 to 40
CAB	44.44	26.67		2.0 to 0.25 to 0.75
ATEC	5.56	3.33		2.0 to 0.25 to 0.75
PEG 400	16.67	10.00		2.0 to 0.25 to 0.75
Total batch	166.67	100.00		
Total coating	66.67			
Acetone	1200.00			
water	0.00			
Coating solution conc	5.26		REDACTED	
Total weight of coating	1266.67			
Take 10 gm at 20 % coating	475.00	20.00		550 → 22%
Take 10 gm at 30 % coating	814.29	30.00		942 → 33%
Final=40 % coating	1266.73	40.00		

REDACTED

FOR UNIGLATT
Date: _____ Lot number: SR1860-41 Equipment number: F-044
Set up (check one): Top spray ☒ Bottom spray (checked) ☒ Bottom spray (cone) ☐
Filter bag: ☒ micronized ☐ screen ☐
Nozzle size (mm): 0.8 1.5 1.2
Plate: ☒ ☐ ☐
Autoshaker: ON OFF
apex: Yes No

Time	Spray rate pellets	PO batch	PO size	Actual discharge (mm. dia)	Outlet Temp. (C)	Inlet Temp. (C)	Outlet dew pt. (C)	Dew pt.	Comments
9:30 am	5.0	50	0	1.5	24	22	10%	52	Batch closed up at 67 gm of light material
10:20	5.0	40	10	1.5	24	20	35%	45	Restart with new pellets
10:35	5.5	50	20	1.5	20	20	35%	43	
11:00	4.0	50	10	1.5	20	20	35%	45	
11:15	4.5	50	110	1.5	20	20	35%	42	
11:30	5.0	50	120	1.5	23	24	35%	42	
12:00 PM	6.5	50	170	1.5	27	30	35%	41	
12:15 PM	5.5	50	180	1.5	28	30	35%	45	
12:30 PM	5.5	50	200	1.5	28	29	35%	43	Take 40 gm sample. 155 gm
1:00 PM	5.5	40	210	1.5	24	28	35%	45	
1:30 PM	5.5	40	290	1.5	25	28	35%	45	Take 40 gm sample. 155 gm
2:15	6.5	50	300	1.5	26	30	35%	45	
3:00	0			1.5	25	28	35%	45	Finish coating at 2:15 and 4 min. (1200 gm) weigh pellets = 127.37 gm

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REDACTED

Date _____

Read and Understood By

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REDACTED

Date _____

REDACTED

gms/batch

1	celphers	ea 203	240
2	Metoprolol succinate		600
3	Methocel	E5	30
4	Tridien 80		0.5
5	Water		1800
Total			870.5

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR1860-42 Equipment number: E-235

Set up (circle one): Top spray (circle one): Bottom spray (circle one): Bottom spray (circle one):

Filter bag: _____ Top spray (circle one): Bottom spray (circle one):

Nozzle size (mm): 1.0 1.2

plate: A B C

column height: _____

paper: _____

Yes No Autochoker: ON OFF

Time	Spray rate (g/min)	FO product	FO rate (g/hr)	Actual throughput (g/min)	Date Temp (°C)	Set Temp (°C)	Out of bag	Down by	Comments
9:45	3.0	0.3	0.2	1.5	50	75	30%	100	
9:55	3.5	0.3	0.2	1.5	50	80	30%	100	
10:10	4.0	0.3	0.2	1.5	50	80	30%	100	
10:25	4.5	0.3	0.2	1.5	50	80	30%	100	
10:40	5.0	0.3	0.2	1.5	50	80	30%	100	
10:55	5.5	0.3	0.2	1.5	50	80	30%	100	
11:10	6.0	0.3	0.2	1.5	50	80	30%	100	
11:25	6.5	0.3	0.2	1.5	50	80	30%	100	
11:40	7.0	0.3	0.2	1.5	50	80	30%	100	
11:55	7.5	0.3	0.2	1.5	50	80	30%	100	
12:10	8.0	0.3	0.2	1.5	50	80	30%	100	
12:25	8.5	0.3	0.2	1.5	50	80	30%	100	
12:40	9.0	0.3	0.2	1.5	50	80	30%	100	
12:55	9.5	0.3	0.2	1.5	50	80	30%	100	
13:10	10.0	0.3	0.2	1.5	50	80	30%	100	
13:25	10.5	0.3	0.2	1.5	50	80	30%	100	
13:40	11.0	0.3	0.2	1.5	50	80	30%	100	
13:55	11.5	0.3	0.2	1.5	50	80	30%	100	
14:10	12.0	0.3	0.2	1.5	50	80	30%	100	
14:25	12.5	0.3	0.2	1.5	50	80	30%	100	
14:40	13.0	0.3	0.2	1.5	50	80	30%	100	
14:55	13.5	0.3	0.2	1.5	50	80	30%	100	
15:10	14.0	0.3	0.2	1.5	50	80	30%	100	
15:25	14.5	0.3	0.2	1.5	50	80	30%	100	
15:40	15.0	0.3	0.2	1.5	50	80	30%	100	
15:55	15.5	0.3	0.2	1.5	50	80	30%	100	
16:10	16.0	0.3	0.2	1.5	50	80	30%	100	

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR1860-42 Equipment number: _____

Set up (circle one): Top spray (circle one): Bottom spray (circle one): Bottom spray (circle one):

Filter bag: _____ Top spray (circle one): Bottom spray (circle one):

Nozzle size (mm): 1.0 1.2

plate: A B C

column height: _____

paper: _____

Yes No Autochoker: ON OFF

Time	Spray rate (g/min)	FO product	FO rate (g/hr)	Actual throughput (g/min)	Date Temp (°C)	Set Temp (°C)	Out of bag	Down by	Comments
6:30	6.0	0.7	1.9	1.5	50	82	30%	100	
7:00	0	0.7	2.1	1.5	50	82	30%	100	Final 30% dry
7:05	Final 30% dry								n = 844.7 g
									Refact n = 6.419

N/A
REDACTED

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Read and Understood By

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Date

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Date

REDACTED

SR1860-43	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	80	SR1860-33	60 to 40
CAB	18.75	15		75 to 10 to 15
ATEC	2.50	2		75 to 10 to 15
Klucel EF	3.75	3		75 to 10 to 15
Total batch	125.00	100		
Total coating	25.00			
Acetone	375.00			
water	75.00			
Coating solution cont	5.25			
Total weight of coating	475.00			
Dissolve Klucel EF in water				
Add acetone into Klucel Solution				
Add CAB and ATEC into Klucel Solution				
Use stir bar to mix solution				

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR1860-43 Equipment number: F-049
 Set up (circle one): Top spray Modified Bottom spray (Murex) Bottom spray (cone)
 Filter bag: _____
 Nozzle size (mm): 0.8 1.3
 plate: _____
 column height: Yes No Autohealer: ON OFF
 spacer: _____

Time	avg pm min	FO prod	FO add at bar	Actual discharge (mm. per)	Gate Temp. °C	Hot Temp. °C	Gate at top	Down to	Comments
12:05	3.0	70	20	1.5	32	31	35%	97	
12:20	3.5	80	20	1.5	34	42	35%	84	
12:35	4.0	90	20	1.5	36	44	35%	82	
12:50	4.5	90	30	1.5	34	42	35%	84	
1:05	5.0	50	70	1.5	34	42	35%	84	
1:20	5.5	40	90	1.6	34	42	35%	84	
1:35	5.5	40	150	1.5	38	42	35%	84	
1:50	5.5	40	160	1.5	34	42	35%	84	
2:05	0	40	180	1.5	34	42	35%	84	small 26.4g
2:20	10.0	100%							11.4g 8.4g

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Date

REDACTED

SR1860-44	gmv/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	80	SR1860-33	60 to 40
CAB	18.75	15		75 to 10 to 15
ATBC	2.50	2		75 to 10 to 15
Klucel EF	3.75	3		75 to 10 to 15
Total batch	125.00	100		
Total coating	25.00			
Acetone	375.00			
water	75.00			
Coating solution conc	5.26			
Total weight of coating	475.00			
Dissolve Klucel EF in water				
Add acetone into Klucel Solution <u>ATBC</u>				
Add CAB and ATBC into klucel Solution				
Use stir bar to mix solution				

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR 1860-44 Equipment number: E-044
 Set up (which one): _____ Top spray: Modified Bottom spray (Wheeler): _____ Bottom spray (cone): _____
 Filter bag: _____ Screen: 1.5
 Nozzle size (mm): 0.8
 plate: _____ Auto: ON OFF
 column height: _____
 speed: _____

Time	dry air inlet	FO inlet	FO outlet	Actual humidity (mm Hg)	Dry Temp. (°C)	Wet Temp. (°C)	Dry at top	Hum by	Comments
7:00	3.0	20	20	1.5	31	38	75%	By	
7:05	3.5	40	20	1.5	31	42	75%	By	
7:10	4.0	50	40	1.5	33	42	75%	By	
7:15	4.5	50	50	1.5	33	40	75%	By	
7:20	5.0	50	60	1.5	32	40	75%	By	
7:25	5.5	70	70	1.5	33	40	75%	By	Some static
7:30	6.5	80	100	1.5	33	40	35%	not	
7:35	5.5	30	110	1.5	33	40	35%	not	
7:40	7	30	100	1.5	33	40	35%	not	Finish 20 min
7:45	Finish drying								n=110-528
									Reject n=7-908

N/A
REDACTED

Continued on Page _____

Read and Understood by

REDACTED

REDACTED

Signed

Date

Signed

Date

REDACTED

SR1860-45	Ingredients	gm/batch	Lot #
1	MS Active Pellets I	435	SR1860-42
2	Meloprolof Succinata	300	611062
3	E5	15	9903005
4	Tween 80	0.25	N/A
5	water	900	
	Total	750.25	RE

REDACTED

REDACTED

Lot number SR186-45

Equipment number: F-115

Get up there, one

Top story

Referral Agency Information

NOTES

Filter bag:

microboards

SECRET

•

Platz der Sitz- und Freizeitanlagen

10. 12.

A

column height:

2601

Autohaker: 1

OFF

[illegible]

REDACTED

Continued on Page

Read and Understood By

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Signed

REDACTED

Date _____

85

Signed

REDACTED

Date _____

SR1860-46	Ingredients	gm/batch	Lot #	gm/actual batch
1	MS Active Pellets I	435	SR1860-42	397.00
2	Metoprolol Succinate	300		273.79
3	E5	15		13.69
4	Tween 80	0.25		0.23
5	water	900		821.38
	Total	750.25		684.71

REDACTED

FOR UNGLATT

Date: _____ Lot number: SR1860-46 Equipment number: F-122

Set up (circle one): _____ Top spray (circle one): Bottom spray (Muster) Bottom spray (cone) _____

Filter type: _____ Nozzle size (mm): 0.8 _____

plate: A _____

column height: Adjusted _____

operator: Yes _____

Automatic: ON _____

Time	Spray rate (ml/min)	FO product	FO added at Bar	Actual distribution (mm. per)	Dwell Temp (°C)	Wet Temp (°C)	Dwell at Top	Time by	Comments
8:40	3.0	0.3	0.2	1.5	50	70	30%	1:10	
9:05	3.5	0.4	0.2	1.5	50	70	30%	1:10	
10:00	6.0	0.7	0.2	1.5	50	70	30%	1:10	
10:25	4.5	0.9	0.2	1.5	50	70	30%	1:10	
10:40	5.0	0.4	0.2	1.5	50	70	30%	1:10	
10:55	5.5	0.5	0.3	1.5	50	70	30%	1:10	
11:00	6.0	0.5	0.4	1.5	50	70	30%	1:10	
11:20	6.0	0.5	0.7	1.5	50	70	30%	1:10	
12:10	1.0	0.5	1.1	1.5	50	70	30%	1:10	
12:40	6.0	0.5	1.3	1.5	50	70	30%	1:10	
1:10	6.0	0.5	1.4	1.5	50	70	30%	1:10	
1:40	6.0	0.5	1.5	1.5	50	70	30%	1:10	
2:00	0	0.5	1.6	1.5	50	70	30%	1:10	Finish drying
2:25	Finish drying								n=674.7 g

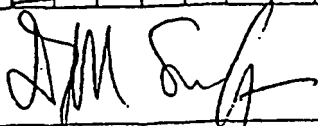
NUMBER OF PLATE 1243-1

D

REDACTED

Continued on Page _____

Read and Understood By



Signed

REDACTED

Date



Signed

REDACTED

Date

REDACTED

SR1860-47	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	82.500	32/180-33	82.5 to 17.5
CAB	15.91	13.125		75 to 10 to 15
ATBC	2.12	1.750		75 to 10 to 15
Klucel EF	3.18	2.625		75 to 10 to 15
Total batch	121.21	100.000		
Total coating	21.21			
Acetone	335.00			
water	65.00			
Coating solution conc	5.04			
Total weight of coating	421.21			
Take 10 gm of sample at 12.5%	283.79			
Take 10 gm of sample at 15.0%	351.50			
Dissolve Klucel EF in water				
Add acetone into Klucel Solution				
Add CAB and ATEC into Klucel Solution				
Use stir bar to mix solution				

REDACTED

FOR UNIGLATT

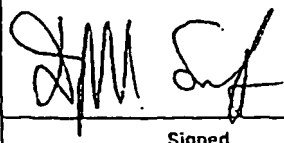
Date: _____ Lot number: SR1860-47 Equipment number: F-129
Set up (circle one): Top spray ☒ Bottom spray (Number) 15 Bottom spray (cone) 1
Filter bag: _____ Nozzle size (mm): 0.8 plate: B Auto heater: ON OFF
solvent height: 20 mm. Yes. No. No Yes

Time	dry on min	FD product	FD air flow	Actual dust flow (g/min)	Tube Temp (°C)	Hot Temp (°C)	Heat at flow	Time by	Comments
3:55	3.0	0.4	0.2	1.5	30	20	30%	100%	
4:11	3.5	0.4	0.2	1.5	30	20	30%	100%	
4:25	4.0	0.4	0.4	1.5	30	20	30%	100%	
4:50	4.5	0.4	0.6	1.5	30	20	30%	100%	
4:55	5.0	0.4	0.8	1.5	29	20	30%	100%	
5:10	5.5	0.4	0.9	1.5	29	20	30%	100%	
5:25	5.5	0.4	1.3	1.5	29	20	30%	100%	Take Sample 12.5%
5:40	5.5	0.4	1.6	1.5	29	20	30%	100%	Take Sample 15.0%
5:55	0	0.4	1.8	1.5	29	20	30%	100%	Finish spraying
6:01	Finish	Reaping							n = 87.90%

Reject n = 65.1%

Continued on Page _____

Read and Understood By



Signed

REDACTED

Date



Signed

REDACTED

Date

REDACTED

SR1860-48	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	82.500	1860-33,45,46	82.5 to 17.5
CAB	18.97	14.000		24 to 3 to 3
ATBC	2.12	1.750		24 to 3 to 3
PEG 400	2.12	1.750		24 to 3 to 3
Total batch	121.21	100.000		
Total coating	21.21			
Acetone	400.00			
water	0.00			
Coating solution conc	5.04			
Total weight of coating	421.21			
Take 10 gm of sample at 12.5%	283.79			
Take 10 gm of sample at 15.0%	351.50			

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR 1860-48 Equipment number: F-125

Set up (circle one): Top spray (circle one): Bottom spray (circle one):
Filter bag: microscreen screen
Nozzle size (mm): 0.8 1.5 2.0
plate: 0 1 2 3 4 5 6 7 8 9
coating height: 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
sprayer: No Auto/stop: ON OFF

Time	dry rate g/min	FD pushed	FD out of the	Actual discharge rate (g/min)	Out Temp. (°C)	Set Temp. (°C)	Out at top (°C)	Done by	Comments
11:50	2.0	0.3	0.2	1.4	30	20	20	---	
11:55	3.5	0.4	0.2	1.5	30	20	20	---	
12:00	0.0	0.4	0.2	1.5	29	20	20	---	
12:05	0.5	0.4	0.4	1.5	29	20	20	---	
12:10	0.0	0.4	0.4	1.5	29	20	20	---	
12:15	5.0	0.4	0.4	1.5	29	20	20	---	Discontinue 12:15 dry
12:25	0	0.4	0.4	1.5	29	20	20	---	Discontinue 12:25 dry
12:30	11-12	0.7							File Sample at 12:30 dry 12:30

NA
REDACTED

Continued on Page _____

Read and Understood By



Signed

REDACTED

Date


Signed

REDACTED

Date

REDACTED

SR1880-49	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	82.500	1660-33,45,46	82.5 to 17.5
CAB	18.97	14.000		24 to 6
ATBC	4.24	3.600		24 to 6
PEG 400	0.00	0.000		
Total batch	121.21	100.000		
Total coating	21.21			
Acetone	400.00			
water	0.00			
Coating solution conc	5.04			
Total weight of coating	421.21			
Take 10 gm of sample at 12.5%	283.78			
Take 10 gm of sample at 15.0%	351.50			

REDACTED

FOR UNIGLATT

Date: _____ Lot number: 521860-49 Equipment number: 52064

Set up (table size): _____ Top spray (micronized) _____ Bottom spray (Munich) _____ Bottom spray (cone) _____

Filter bag: _____ Screen _____

Nozzle size (mm): 3.0 B C D

plate: 2 A B C D

column height: _____ Autoheating: ON OFF

spacer: Yes No

Time	spg rate ml/min	FD product	FD rate of bar	Atom structure (mm bar)	Dist from FD	Int from FD	Dist at top	Dist by	Comments
10:55	3.0	2.0	1.0	1.5	28	30	2.8	ml/min	
11:00	3.5	3.0	1.5	1.5	27	30	3.0	ml/min	
11:25	3.0	3.0	2.0	1.5	27	30	3.0	ml/min	
11:40	3.5	3.0	4.0	1.5	26	30	3.0	ml/min	
11:55	5.0	5.0	6.0	1.5	26	30	3.0	ml/min	
12:25	5.0	3.0	1.0	1.5	26	30	3.0	ml/min	Take sample at 12:16 min
12:48	0	3.0	1.0	1.5	26	30	3.0	ml/min	Take sample at 12:30 min
12:53	finish	ending							93.80 g

N/A
REDACTED

Continued on Page _____

Read and Understood By

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REDACTED

Date

Signed

REDACTED

Date

SR1860-62	Ingredients	gm/batch
9611005	1 Sugar Sphere 60/80	240
011062	2 Metoprolol Succinate	600
9903005	3 E5	30
n/a	4 Tween 80	0.5
	5 water	1800
	5 Total	870.5

REDACTED

FOR UNIGLATT

Date: Lot number: SR1860-62 Equipment number: F-125

Set up (circle one):

Filter bag:

Nozzle size (mm):

plate:

column height:

spacer:

Top spray

micronized

0.8

A

24.00

Yes

Bottom spray (Wurster)

screen

1.0

B

C

No

Bottom spray (cone)

D

OFF

Autoshaker: ON

OFF

Time	spray rate ml/min	FD product	FD add at 100	Actual concentration from 100	Outlet Temp. °C	Inlet Temp. °C	Outlet at 100	Dose by	Comments
10:05	2.0	0.4	0.2	1.5	49	70	30%	MF	
10:35	2.5	0.4	0.5	1.5	50	70	30%	MF	
11:05	3.0	0.4	0.6	1.5	50	68	30%	MF	
11:35	3.5	0.4	0.9	1.5	49	69	30%	MF	
12:05	4.0	0.4	1.4	1.5	49	70	30%	MF	
12:35	4.5	0.4	1.2	1.5	49	70	30%	MF	
1:05	5.0	0.4	1.2	1.5	48	72	30%	MF	
1:35	5.5	0.5	1.4	1.5	48	72	30%	MF	
2:05	6.0	0.5	1.4	1.5	49	72	30%	MF	
2:35	6.0	0.5	1.6	1.5	48	72	30%	MF	
3:05	6.0	0.5	1.8	1.5	48	72	30%	MF	
3:35	6.0	0.5	1.9	1.5	47	72	30%	MF	
4:05	6.0	0.5	2.1	1.5	48	72	30%	MF	
4:35	6.0	0.5	2.6	1.5	48	72	35%	MF	
6:00	60	0.6	2.8	1.5	52	72	35%	MF	on #30 = 46.4g Thru #20 = 782.1g Total = 828.5g 95.2% yield Some pellets and powder on outlet filter.

Continued on Page

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Date

Signed

Date

SR1860-64	Ingredients	gm/batch	Lot #
1	Metoprolol Succinate Active pellets I	435	SR1860-62
2	Metoprolol Succinate	300	011062
3	E5	15	9903005
4	Tween 80	0.25	N/A
5	water	900	
5	Total	750.25	REDACTED

REDACTED

FOR UNGLATT

Date: _____

Lot number: SR1860-62Equipment number: E-125

Set up (circle one):

Top spray

Bottom spray (Wurster)

Bottom spray (cone)

Filter bag:

Microfines

screen

Nozzle size (mm):

0.8

1.0

plate:

A

B

C

D

column height:

25 mm

No

space:

Yes

No

Autobaker: ON OFF

Time	spray rate ml/min	PD product	PD code of lot	Actual standards prod. (mg)	Dist. Temp. °C	Int. Temp. °C	Dist. at top °C	Done by	Comments
11:00	2.0	0.4	0.2	1.5	48	72	39%	MC	
11:40	2.5	0.4	0.8	1.5	49	70	39%	MC	
12:10	3.0	0.5	1.5	1.5	48	71	39%	MC	
12:55	3.5	0.5	1.5	1.5	48	69	39%	MC	
1:25	4.0	0.5	2.2	1.5	48	70	39%	MC	
1:55	4.5	0.5	2.6	1.5	48	72	39%	MC	
2:25	5.0	0.5	2.8	1.5	48	70	39%	MC	
2:55	5.5	0.5	2.9	1.5	48	74	39%	MC	
3:25	6.0	0.5	3.1	1.5	48	73	39%	MC	
3:55	6.0	0.5	3.2	1.5	48	72	39%	MC	
4:12	0	0.5	3.4	1.5	48	70	39%	MC	Final 30 min
4:27	Final 30 min								N=660.8g

N

A-REDACTED

Continued on Page _____

Read and Understood By

Signed

Date

Signed

Date

SR1860-71	Ingredients	gm/batch	Lot #
1	Metoprolol Succinate Active pellets I	340.00	SR1860-62
2	Metoprolol Succinate	234.48	011062
3	E5	11.72	9903005
4	Tween 80	0.20	
5	water	703.45	
5	Total	586.40	

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR1860-71 Equipment number: E-125

Set up (circle one): Top spray micronized Bottom spray (Wurster) Bottom spray (cone)
Filter bag: _____
Nozzle size (mm): 0.8 1.0 1.2
plate: A B C D
column height: 2.0 2.5 3.0 3.5 4.0 4.5 5.0
sprayer: Yes No Autoshears: ON OFF

Time	Spray rate g/min	PD product	PD outlet	Actual atomization pressure (bar)	Outlet Temp. (C)	Inlet Temp. (C)	Outlet at top	Done by	Comments
10:30	3.0	0.4	0.2	1.5	50	70	35%	MCB	
10:45	3.5	0.4	0.2	1.5	50	70	35%	MCB	
11:00	4.0	0.4	0.2	1.5	50	69	35%	MCB	
11:15	4.5	0.4	0.2	1.5	50	68	35%	MCB	
11:30	5.0	0.4	0.7	1.5	50	67	35%	MCB	
11:45	5.5	0.6	1.1	1.5	50	70	35%	MCB	
12:00	6.0	0.5	1.5	1.5	50	70	35%	MCB	
12:00	6.0	0.5	1.5	1.5	50	70	35%	MCB	
1:10	0	0.5	2.5	1.5	50	70	35%	MCB	Finish spraying n=547.9 g
1:15	Finish drying								Refect n=23.1 g

REDACTED

Continued on Page _____

Read and Understood By

SR REDACTED

Signed _____ Date _____

SR

Signed _____ Date _____

REDACTED

Date _____

SR1860-72	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	60.000	1860-64	
CAB	56.67	34.000	92-00257	85 to 15
Lutrol F-68 (Pluronic F-68)	10.00	6.000	WPEV-558	85 to 15
HPC	0.00	0.000		
Total batch	166.67	100.000		
Total coating	66.67			
Acetone	1200.00			
water	125.00			
Coating solution conc	5.03			
Total weight of coating	1391.67			
Take 10 gm of sample at 30%	895.02			

REDACTED

FOR UNIGLATT

Date: Lot number: SR1860-72 Equipment number: E-044

Set up (circle one): Top spray micronized Bottom spray (Wurster) Bottom spray (cone)
 Filter bag: screen 1.0 1.2
 Nozzle size (mm): 0.8 B C D
 plate:
 column height: 20 mm
 upwrap: Yes No Autosampler: ON OFF

Time	spray rate ml/min	PO product	PO outlet at flow	Actual standards from flow	Outlet Temp. °C	Wet Temp. °C	Outlet at top	Done by	Comments
10:10	3.0	50	10	1.5	28	22	30%	MCB	
10:25	3.5	50	10	1.5	26	22	3%	MCB	
10:40	4.0	50	20	1.5	26	22	30%	MCB	
10:55	4.5	50	50	1.5	25	21	30%	MCB	
11:10	5.0	40	80	1.5	25	21	30%	MCB	
11:25	5.5	40	90	1.5	25	21	60%	MCB	
11:40	6.0	40	160	1.5	25	21	30%	MCB	
12:10	6.0	40	160	1.5	25	21	30%	MCB	
12:40	6.0	40	170	1.5	25	21	30%	MCB	
1:10	6.0	40	200	1.5	25	21	30%	MCB	Take sample at 10:28
1:40	6.0	40	240	1.5	25	21	3%	MCB	
2:10	6.0	40	350	1.5	25	21	30%	MCB	
2:28	0	40	400	1.5	25	21	30%	MCB	Finish spraying
2:33	Finish spraying								W=118.0 g
									Reject 11-226 g

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Read and Understood By

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REDACTED

Signed

REDACTED

Date

SR1860-74	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	60.000	1860-64	
CAB	60.00	36.000	1860-64	90 to 10
Lutrol F-68 (Pluronic F-68)	6.67	4.000	1860-64	90 to 10
HPC	0.00	0.000		
Total batch	166.67	100.000		
Total coating	66.67			
Acetone	1200.00			
water	125.00			
Coating solution conc	5.03			
Total weight of coating	1391.67			
Take <u>10</u> gm of sample at 30%	895.02			

REDACTED

FOR UNIGLATT

Date: _____ Lot number: SR1860-74 Equipment number: E-125

Set up (circle one):

Filter bag:

Nozzle size (mm):

plate:

column height:

spacer:

Top spray

micronized

0.8

A

24.00

Yes

Bottom spray (Wurster):

screen

1.0

B

No

No

Equipment number:

E-125

Bottom spray (cone)

C

Autoshaker: ON

OFF

Time	Spray rate ml/min	PU product	PU inlet at 100	Actual concentration press. (bar)	Duct Temp. °C	Inlet Temp. °C	Duct at 100	Done by	Comments
10:55	3.0	0.5	0.3	1.5	27	21	35%	WFO	
11:11	3.5	0.6	0.3	1.5	28	20	35%	WFO	
11:25	4.0	0.6	0.4	1.5	28	20	35%	WFO	
11:41	4.4	0.5	0.5	1.5	28	20	30%	WFO	
11:55	5.0	0.5	0.7	1.5	28	20	30%	WFO	
12:10	5.5	0.5	0.7	1.5	28	20	30%	WFO	
12:25	6.0	0.4	0.9	1.5	28	20	30%	WFO	
12:38	6.0	0.4	1.3	1.5	28	20	30%	WFO	
1:25	6.0	0.4	1.6	1.5	28	20	30%	WFO	
1:55	6.0	0.4	1.9	1.5	28	20	30%	WFO	
2:25	6.0	0.4	2.2	1.5	28	20	30%	WFO	Take sample 235 gm
2:55	6.0	0.4	2.5	1.5	28	20	30%	WFO	
3:25	6.0	0.4	2.8	1.5	28	20	30%	WFO	
3:55	6.0	0.4	3.1	1.5	28	20	30%	WFO	
4:07	0	0.4	3.3	1.5	28	20	30%	WFO	Finish spraying
4:10	Finish spraying								WFO 120.80 g
									Reject n=21.98

Continued on Page _____

Read and Understood By

REDACTED

REDACTED

Signed

Date

Signed

Date

PROJECT Metoprolol succinate ER pelletsNotebook No. SR1860
Continued From Page

75

SR1860-75	gm/batch	%	Lot #	Ratio
Metoprolol Succinate pellets	100.00	60.000	1860-64	
CAB	63.33	38.000	WPCV-583	95 to 5
Lutrol F-68 (Pluronic F-68)	3.33	2.000	WPCV-583	95 to 5
HPC	0.00	0.000		
Total batch	166.67	100.000		
Total coating	66.67			
Acetone	1200.00			
water	125.00			
Coating solution conc	5.03			
Total weight of coating	1391.67			
Take 10 gm of sample at 30%	895.02			

REDACTED

FOR UNIGLATT

Date:

Lot number: 2LX60-75Equipment number: F-044

Set up (circle one):

Filter bag:

Nozzle size (mm):

plate:

column height:

space:

Top spray

micronized

0.8

A

20 mm

Yes

Bottom spray (Wurster)

screen

1.8

B

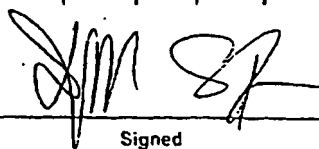
Autoshaker: ON

Bottom spray (cone)

Time	Spray rate ml/min	PD product	PD inlet air flow	Actual atomization (mm, bar)	Duct Temp. °C	Inlet Temp. °C	Duct air flow	Done by	Comments
1:35	3.0	70	10	1.5	29	29	30%	WCP	
1:50	3.5	100	50	1.5	27	22	30%	WCP	
2:10	4.0	90	90	1.5	27	22	30%	WCP	
2:25	4.5	60	130	1.5	27	22	30%	WCP	
2:45	5.0	50	100	1.5	27	22	30%	WCP	STOP AND RESTORE AT 2:45
3:00	5.5	30	180	1.5	26	22	30%	WCP	THRU TO FLAKEL Column
3:15	6.0	30	210	1.5	26	22	30%	WCP	
3:45	6.0	30	280	1.5	26	22	30%	WCP	
4:15	6.0	30	350	1.5	26	22	30%	WCP	
4:45	6.0	30	370	1.5	26	22	30%	WCP	
5:35	6.0	30	410	1.5	26	22	30%	WCP	STOP SPRAYING
8:35	6.0	40	450	1.5	28	27	30%	WCP	RESTART AT 8:35 AM
9:05	6.0	40	500	1.5	26	22	30%	WCP	
9:35	6.0	30	470	1.5	26	22	30%	WCP	
10:05	6.0	30	510	1.5	26	22	30%	WCP	
10:28	0	30	510	1.5	26	22	30%	WCP	FINISH SPRAYING
10:33	Flow stop	Drying							11:16:67
									Reject = 5.4 g

Continued on Page

Read and Understood By



Signed

REDACTED

Date



Signed

REDACTED

Date

REDACTED

Metoprolol Succinate ER Pellets, 190 mg

Lot# SR1860-36(30%)

Dissolution (n=2) in SGF, pH7.5

Lot # SR 1860-36(30%)

USP App. 2

75 rpm

SGF

Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	*	0	0	15	0	0
0.5	2	*	1	1	16	1	2
1	3	*	2	3	9	2	3
2	6	*	5	5	7	5	6
4	22	*	18	20	12	18	22
6	49	*	42	45	10	42	49
8	69	*	63	66	7	63	69
12	90	*	86	88	3	86	90
16	98	*	95	97	2	95	98

* Data not used. The amount of pellets poured into the vessel was doubled.

Lot # SR 1860-36(30%)

USP App. 2

75 rpm

pH7.5

Hanson

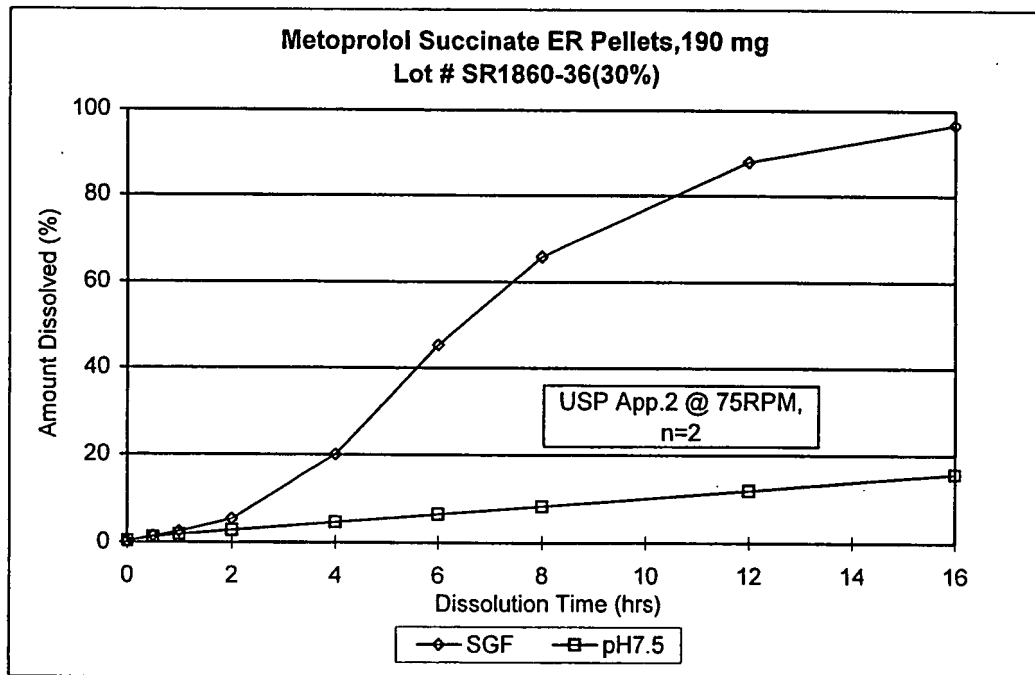
UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	^	0	18	0	0
0.5	1	1	^	1	17	1	1
1	2	2	^	2	12	2	2
2	3	3	^	3	7	3	3
4	5	5	^	5	2	5	5
6	6	7	^	7	1	6	7
8	8	8	^	8	1	8	8
12	12	12	^	12	2	12	12
16	15	16	^	16	2	15	16

^ Data not used. Pellets were not poured into the vessel.



REDACTED

Metoprolol Succinate ER Pellets, 190 mg

Lot# SR1860-36(20%)

Dissolution (n=3) in SGF, pH7.5

Lot # SR 1860-36(20%)

USP App. 2

75 rpm

SGF

Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	-1275	0	0
0.5	2	1	2	1	50	1	2
1	27	15	13	18	41	13	27
2	80	65	58	68	17	58	80
4	98	90	86	92	6	86	98
6	101	94	92	96	5	92	101
8	102	97	95	98	4	95	102
12	103	99	97	100	3	97	103
16	104	100	98	101	3	98	104

Lot # SR 1860-36(20%)

USP App. 2

75 rpm

pH7.5

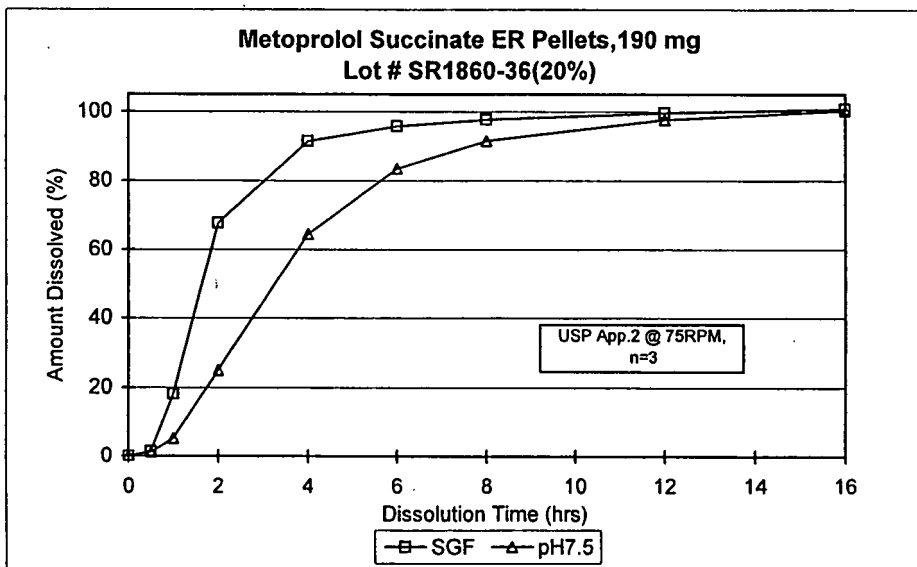
Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	31	0	0
0.5	1	2	1	1	31	1	2
1	5	5	6	5	8	5	6
2	24	21	29	25	17	21	29
4	64	58	71	64	10	58	71
6	84	78	88	84	6	78	88
8	92	88	95	92	4	88	95
12	98	95	100	98	3	95	100
16	101	98	102	100	2	98	102



REDACTED

Metoprolol Succinate ER Pellets, 190 mg

Lot# SR1860-39 (40%)

Dissolution (n=3) in SGF and pH7.5 Buffers

Lot #SR1860-39 (40%)

USP App. 2

75 rpm

SGF

Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	10	11	12	11	9	10	12
0.5	31	32	34	32	4	31	34
1	49	50	52	50	2	49	52
2	75	75	76	75	1	75	76
4	95	94	95	95	0	94	95
6	100	100	100	100	0	100	100
8	103	102	102	102	0	102	103
12	105	104	103	104	1	103	105
16	105	104	104	104	1	104	105

Lot #SR1860-39 (40%)

USP App. 2

75 rpm

pH7.5

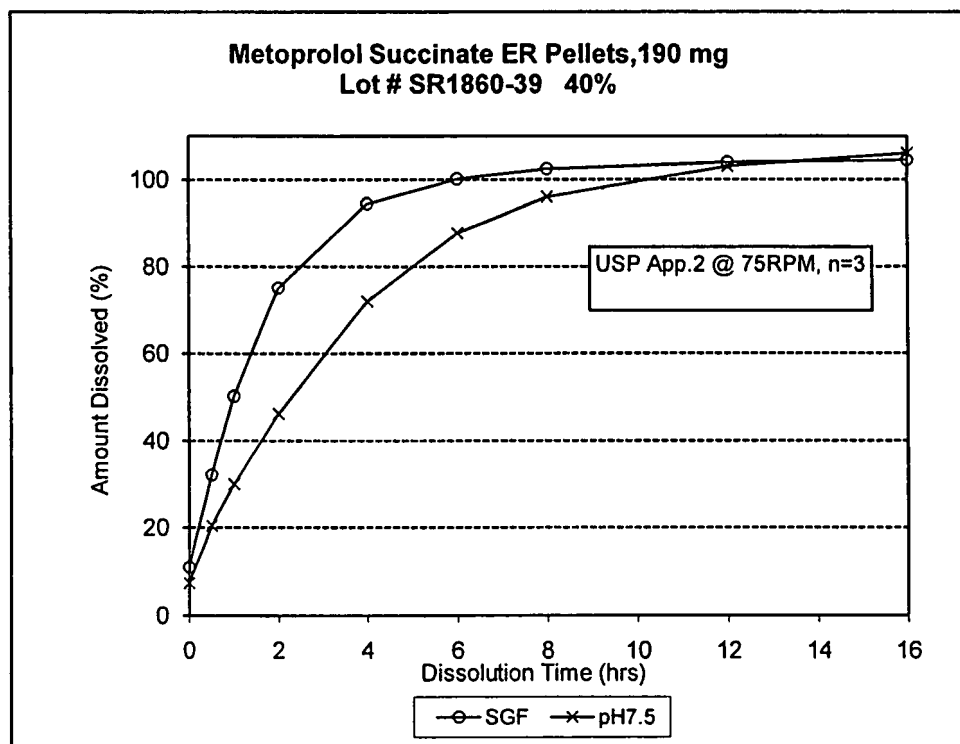
Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	8	7	7	7	9	7	8
0.5	22	21	19	20	7	19	22
1	31	30	28	30	5	28	31
2	48	47	44	46	4	44	48
4	74	73	69	72	3	69	74
6	89	88	86	88	2	86	89
8	97	96	95	96	1	95	97
12	104	103	102	103	1	102	104
16	107	106	105	106	1	105	107



REDACTED

Metoprolol Succinate ER Pellets, 190 mg

Lot# SR1860-38 (30%)

Dissolution (n=3) in SGF, pH4.5, pH6.8, and pH7.5 Buffers

Lot #SR1860-38 (30%)

USP App. 2

75 rpm

SGF

Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	21	20	16	19	12	16	21
0.5	64	66	58	62	7	58	66
1	85	87	80	84	4	80	87
2	99	100	96	99	2	96	100
4	104	105	102	104	1	102	105
6	105	106	104	105	1	104	106
8	106	106	104	105	1	104	106
12	106	107	104	106	1	104	107
16	106	106	104	106	1	104	106

Lot #SR1860-38 (30%)

USP App. 2

75 rpm

pH7.5

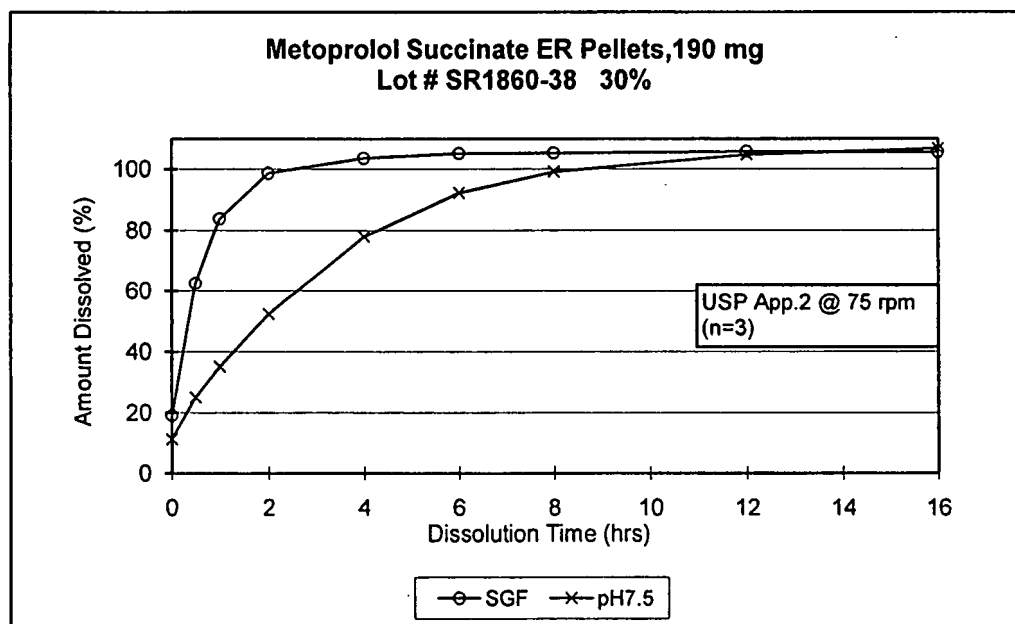
Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)

Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	12	11	10	11	9	10	12
0.5	26	24	24	25	4	24	26
1	36	34	35	35	3	34	36
2	54	51	52	52	3	51	54
4	79	76	78	78	2	76	79
6	93	91	93	92	2	91	93
8	100	98	99	99	1	98	100
12	106	104	105	105	1	104	106
16	108	106	107	107	1	106	108



REDACTED

Metoprolol Succinate ER Tablets, 190 mg

Lots: SR1860-63 #27 #28#29#30

Dissolution (n=3) in pH 7.5 Potassium Phosphate Buffer

Lot # SR1860-63 #27

USP App. 2

75 rpm

pH 7.50

Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	1	0	87.8	0	1
0.5	14	17	16	16	8.9	14	17
1	30	36	32	33	8.5	30	36
2	56	65	60	61	7.4	56	65
4	78	91	84	84	7.8	78	91
6	82	96	90	89	8.1	82	96
8	83	97	91	90	8.1	83	97
12	83	98	91	91	8.0	83	98
16	83	97	91	90	8.0	83	97

Lot # SR1860-63 #28

USP App. 2

75 rpm

pH 7.50

Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	117.7	0	0
0.5	17	20	15	17	15.5	15	20
1	35	40	30	35	13.9	30	40
2	64	71	56	64	12.0	56	71
4	89	98	78	88	11.1	78	98
6	94	103	83	93	11.1	83	103
8	95	105	84	95	11.0	84	105
12	96	105	84	95	11.0	84	105
16	95	105	84	94	11.1	84	105

Lot # SR1860-63 #29

USP App. 2

75 rpm

pH 7.50

Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	-33.1	0	0
0.5	15	15	15	15	2.2	15	15
1	31	31	31	31	0.7	31	31
2	57	58	57	58	1.0	57	58
4	78	80	78	79	1.3	78	80
6	82	84	82	83	1.3	82	84
8	83	85	84	84	1.2	83	85
12	83	85	84	84	1.2	83	85
16	83	85	84	84	1.2	83	85

Lot # SR1860-63 #30

USP App. 2

75 rpm

pH 7.50

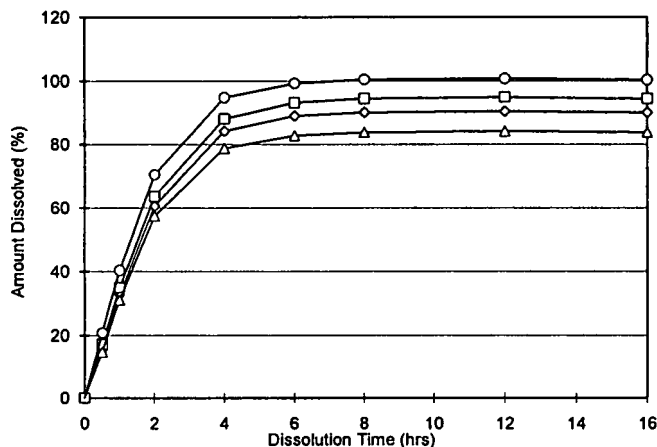
Hanson

UV Analysis: 280nm

Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	-17.5	0	0
0.5	20	20	23	21	7.2	20	23
1	39	40	42	40	4.8	39	42
2	68	71	72	70	2.9	68	72
4	92	96	96	95	2.2	92	96
6	97	101	100	99	2.0	97	101
8	98	102	101	101	2.0	98	102
12	99	102	101	101	1.9	99	102
16	98	102	101	100	2.0	98	102

Metoprolol Succinate ER Tablets, 190 mg
in pH 7.5 Potassium Phosphate Buffer



Lot # SR1860-63 #27 Lot # SR1860-63 #28
Lot # SR1860-63 #29 Lot # SR1860-63 #30

REDACTED

Metoprolol Succinate ER Tablets, 190 mg
Lots: SR1860-72 30%-40% & SR1860-63 #25 #26
Dissolution (n=3) in pH 7.5 Potassium Phosphate Buffer

Lot # SR1860-72 30%
USP App. 2
75 rpm
pH 7.5
Hanson
UV Analysis: 280nm
Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	#DIV/0!	0	0
0.5	8	8	7	8	7.5	7	8
1	29	29	27	28	4.1	27	29
2	70	71	68	70	2.2	68	71
4	98	99	98	98	0.6	98	99
6	102	103	102	102	0.6	102	103
8	103	104	103	103	0.6	103	104
12	104	104	103	104	0.6	103	104
16	104	105	104	104	0.6	104	105

Lot # SR1860-72 40%
USP App. 2
75 rpm
pH 7.5
Hanson
UV Analysis: 280nm
Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	#DIV/0!	0	0
0.5	3	3	2	3	21.7	2	3
1	9	9	7	8	13.9	7	9
2	25	26	23	25	6.3	23	26
4	60	62	57	60	4.2	57	62
6	82	83	80	82	1.9	80	83
8	91	92	89	91	1.7	89	92
12	95	96	95	95	0.6	95	96
16	96	97	96	96	0.6	96	97

Lot # SR1860-63 #25
USP App. 2
75 rpm
pH 7.5
Hanson
UV Analysis: 280nm
Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	#DIV/0!	0	0
0.5	17	17	19	18	6.5	17	19
1	37	37	39	38	3.1	37	39
2	70	69	73	71	2.9	69	73
4	98	97	101	99	2.1	97	101
6	104	103	108	105	2.5	103	108
8	107	105	111	108	2.8	105	111
12	108	107	112	109	2.4	107	112
16	109	108	113	110	2.4	108	113

Lot # SR1860-63 #26
USP App. 2
75 rpm
pH 7.5
Hanson
UV Analysis: 280nm
Cellpath: 10.0mm

Amount Dissolved (%)							
Time (hr)	V1	V2	V3	Mean	%RSD	Min	Max
0	0	0	0	0	#DIV/0!	0	0
0.5	15	15	12	14	12.4	12	15
1	33	31	28	31	8.2	28	33
2	63	59	56	59	5.9	56	63
4	88	82	79	83	5.5	79	88
6	93	87	84	88	5.2	84	93
8	95	88	86	90	5.3	86	95
12	96	89	87	91	5.2	87	96
16	97	90	88	92	5.2	88	97

Metoprolol Succinate ER Tablets, 190 mg
In pH 7.5 Potassium Phosphate Buffer

